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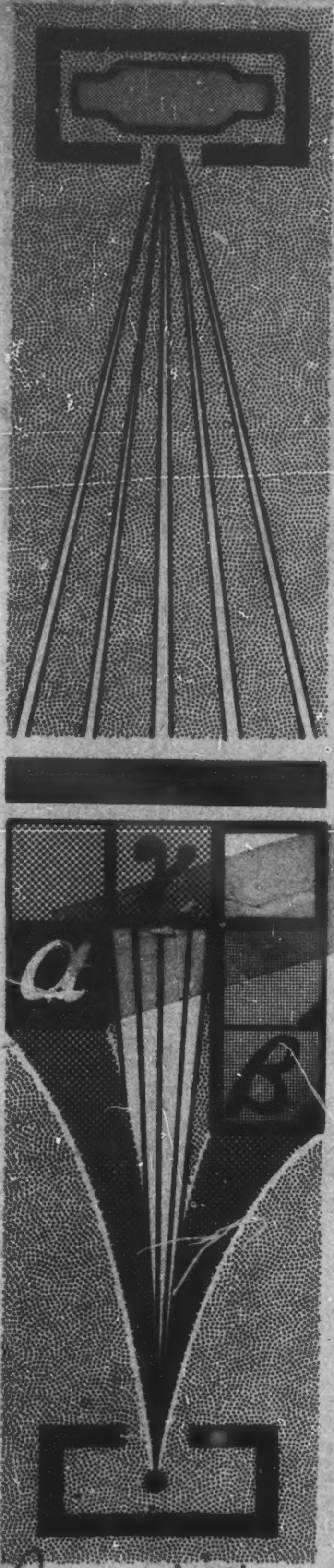

AFTERLOADING IN RADIOTHERAPY

Proceedings of a Conference
held in New York City,
May 6-8, 1971

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AFTERLOADING IN RADIOTHERAPY

Proceedings of a Conference held in New York City, May 6-8, 1971

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Funded under PHS Contract No. 68-05-0001
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Rockville, Maryland 20852

FOREWORD

The Bureau of Radiological Health implements a national program designed to reduce the exposure of man to hazardous ionizing and non-ionizing radiation.

Within the Bureau, the Division of Medical Radiation Exposure deals with 1) the reduction of unproductive ionizing radiation exposure of patients, workers and others exposed by the use of x rays and other machine-produced ionizing radiation, radioactive materials and radiopharmaceuticals, and 2) the improvement of radiological "systems" and methodology in the healing arts. A number of projects and studies are aimed at assessing and minimizing radiation exposure in the healing arts and increasing efficiency in the use of radiation in clinical practice. Several projects are directed toward assessing and improving the qualifications of x-ray users in the healing arts.

Results of intramural and contractor projects of general interest are published as technical reports by the Division of Medical Radiation Exposure and distributed to State and local radiological health program personnel, Bureau technical staff and advisory committee members, university radiation safety officers, libraries and information services, industry, hospitals, laboratories, schools, the press and other interested individuals.

Contract reports on highly specialized topics are printed and distributed without editorial revision. Copies of both general interest and limited distribution reports may be purchased from the National Technical Information Service.

I encourage the readers of these reports to inform the Bureau of any omissions or errors. Your additional comments or requests for further information are also solicited.

John C Villforth

John C. Villforth
Director
Bureau of Radiological Health

PREFACE

It was the objective of this conference to present and discuss the status of afterloading in the interstitial and intracavitary treatment of cancer in the United States and other countries, with special consideration given to radiation protection and control factors. The speakers included prominent scientists from England, France, Italy, Sweden, Bulgaria, Israel, Yugoslavia, and Mexico, as well as spokesmen for the scientific community and various government agencies in the United States. More than 500 people attended the meeting.

The first session of the conference was devoted to discussions of the hazards of radium and radium substitutes in the treatment of cancer, the development and current status of afterloading techniques in various nations, and the use of computers in radiotherapy. Speakers at the second session discussed dosimetry, treatment of cancer of the uterus, and interstitial techniques. In the third session, there was an open discussion on standardization of afterloading sources.

The formal papers elicited considerable comment, rebuttal, and discussion from the audience. During the discussion on standardization of sources, an effort was made to obtain a consensus from the participants. The reader is particularly encouraged to read this discussion. These proceedings include the formal presentations, edited transcripts of the discussions, and an appendix containing presentations by representatives of commercial suppliers of afterloading materials and equipment.

The conference chairman and editor of the proceedings was Dr. Norman Simon and the conference coordinators were Dr. Sidney M. Silverstone and Dr. John Boland, all of The Mount Sinai School of Medicine. Mr. Gail D. Schmidt was project officer for the Division of Medical Radiation Exposure, Bureau of Radiological Health.

Arve H. Dahl
Acting Director
Division of Medical Radiation Exposure

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SELECTED VIEWPOINTS

Some noteworthy points raised at the conference are summarized below:

Status of Afterloading

(1) Simple afterloading has been shown to produce efficacious results and is generally accepted, using either radium or cesium for intracavitary treatments and iridium interstitially. Afterloading provides enhanced radiation protection and allows better source placement.

(2) High intensity remote afterloading is a technique currently under development. It should probably be limited to large sophisticated centers. The approach has the potential to eliminate radiation exposure to hospital staff.

(3) In using californium, afterloading is necessary for radiation protection purposes. This radionuclide is in a developmental stage and requires considerable technical competence regarding the dosimetry of both neutron and gamma photons.

Problems of Brachytherapy

(1) Locating and defining the tumor are some of the major problems which limit effectiveness of treatment.

(2) A related difficulty is the problem of achieving and maintaining proper source location during the treatment period.

Recommendations

(1) Within five years radium should be replaced by cesium or other radioisotopes, in sealed sources.

(2) All radium plaques, nasopharyngeal applicators, and radon seeds should be withdrawn from use.

(3) Computer analysis of dosimetry is considered useful, except for simple applications with fixed activity. Facilities for centralized computer analysis are available.

(4) A simple afterloading system for treating cancer of the uterine cervix is needed in developing nations.

(5) Treatment facilities should have the capability to measure the activity of sources and check their homogeneity.

(6) Standards are needed for sources used in afterloading, specifying strength, leakage, shielding, and other aspects.

OPENING SESSION

OPENING REMARKS

Norman Simon, M.D.

The time is ripe for a conference on afterloading.

Public and professional concern regarding the harmful effects of pollutants has intensified, and our attention is now directed toward ionizing radiation as a pollutant. Whether those who attribute excessive permissiveness to our regulations for radiation protection are right or wrong, it is prudent to reduce exposure to the minimum level necessary for the job. Afterloading is a procedure for placing hollow devices and containers into tumors; the radioactive material is subsequently placed into these containers, thus reducing or even eliminating irradiation to anyone but the patient.

But radiation protection is not the only purpose of afterloading. Accuracy in the surgical placement of the tubes and capsules is improved since the radiotherapist or surgeon is not harassed by the presence of radioactive materials during the more difficult stage of the procedure.

Burgeoning experience with new radionuclides, modern physical data, manufacture, and clinical experimentation makes it necessary to establish the status of applicability of radium substitutes. Radium itself is limited in its adaptability to afterloading and remote loading, but the way now is paved for the use of the newer isotopes.

Brachytherapy with radioactive materials at short distance -- intracavitary or by implantation -- has fallen into disfavor in sophisticated medical centers where megavoltage is stressed. In addition, skilled surgeons are trained to do extensive radical procedures on tumors that formerly were more frequently treated with radium. A generation of radiotherapists have stood by and seen their surgical skills in brachytherapy diminish; they have had little enthusiasm for operative procedures that expose them and their assistants to radium, particularly when an external beam or even excisional surgery would suffice. Now the tables are turned, the development of afterloading has focused attention again on brachytherapy.

Is the current interest in afterloading justified? The purpose of this conference is to help us answer that question. The attendance certainly indicates the extent of professional interest in afterloading.

After a presentation by Dr. Boland of the role of radium and its substitutes in the treatment of cancer, the characteristics of radium (including exposure), the magnitude of the health problem, and a comparison with cesium 137 will be discussed. Then our colleagues from overseas -- England, France, Italy, Latin America, and the Socialist nations -- will present the status of afterloading in their geographic areas.

Since computer technology has become a part of our lives, the next session will be devoted to the applicability of various computer methods and devices to afterloading.

The following session will be comprised of a discussion of afterloading in the treatment of cancer of the cervix -- a disease that is important because of its high incidence, curability, and amenability to brachytherapy with afterloading. The role of afterloading in this disease alone would warrant a conference study.

Cancer of the body of the uterus has been treated for decades with various combinations of surgery and radiation, including external beam, packing with Heyman capsules, and adaptation of these techniques. The presentations here will consider the role of afterloading.

Description of the implantation of tumors by means of afterloading will include a discussion of gamma emitters, with which we are all familiar. We will also learn of recent developments in the use of the neutron-emitting californium 252, a radionuclide whose very life is wedded to afterloading.

Fundamentals of dosimetry, factors controlling safety, and the original systems of dosage that make intracavitary and implantation techniques reproducible and useful will be presented by the pioneers of these important concepts.

Producers and manufacturers of afterloading and remote loading devices will present materials available here and abroad.

The conference will end with an attempt to arrive at conclusions regarding the status of afterloading. It is difficult, even for the experienced radiologist, to select the system, the isotope, and the device that will optimize treatment. Thoughts about these features have preoccupied the working party of the British Institute of Radiology, as well as cancer institutes and individuals in many parts of the world. Opinions will be expressed and questions answered in the last session, and members of the audience may participate.

During the conference written questions directed to the speakers will be accepted by the chairmen. Some of the answers will be reserved for the final day of the conference.

GREETINGS

Dean George James

The venue of this conference had to be changed from our own Mount Sinai School of Medicine to the Hilton Hotel because of an unanticipated but gratifying response from medical people who are particularly interested in the radiation treatment of cancer. There are more than 400 registrants for this meeting. We have a number of illustrious speakers, authorities on the use of radiation in cancer and on applied radiation research in the treatment of cancer. However, we did not anticipate such a response from radiotherapists and physicists, some from great distances.

Afterloading in radiotherapy is of natural interest to the United States Public Health Service, for the Bureau of Radiological Health of the USPHS is charged with promoting radiation safety. In afterloading there is safety. At the Mount Sinai Hospital our interest in afterloading has been similarly in safety, and in accuracy of use of radioactive materials in the treatment of cancer.

I am sorry that our great new facility, a medical school building supported by the good wishes of so many of our friends, cannot be used yet for such a conference as this. I hope that our visitors from England, France, Italy, Yugoslavia, Bulgaria, Mexico, Guatemala, Venezuela, and the United States will profit from this meeting, and that our deliberations will result in benefits for the patients as well as the attendees.

Pioneers in the field of radiation protection are among us (Parker of Battelle and Quimby of Columbia); masters of treatment of cancer in women are here (Kottmeier of Sweden, Gusberg of New York); protectors of the public health are with us (Harley of the AEC and Blatz of the New York Office of Radiation Control); expert radiotherapists from the continent are represented (Chassagne from Gustav-Roussy in Paris, Snelling of London, Sahatchiev of Bulgaria, and others).

We are pleased to cosponsor this meeting with the U. S. Public Health Service, and we hope your discussions and publication will provide decisions helpful in the treatment of individual patients and useful in the important problem of reducing the exposure of personnel radiation.

THE CHALLENGE

Raymond T. Moore, M.D.

Today we find throughout the country a renewed national movement concerned with conservation. Our citizens are demanding that government assure planned management of our resources to prevent their exploitation, their destruction, or their neglect. We in public health feel this directive most strongly, since we view man and his well-being as our most vital resource.

This public concern has strongly affected the area of radiation. Nuclear energy has always raised, in the layman, a vision of destruction of devastating magnitude. In general, the public has trusted government controls and policies in this area. Over the last 20 years we have seen the positive effects of nuclear energy in the civilian economy. But behind the positive impact lies the specter of its destructiveness and this has been magnified, not as it exists, not as it compares with other hazards, but only what it might represent. In this uncertainty, there has arisen renewed emphasis on the need of government to protect man from the potential hazards of radiation.

As you are aware, much attention has been focused on nuclear power plants, their radioactive release, and possible consequence. However, even more recently there have been editorials in the news media as well as in medical journals such as JAMA asking that unnecessary diagnostic radiation exposure be reduced through greater concern and self-policing by the medical community. The International Commission on Radiological Protection has summarized the basis for this concern in their publication No. 16: ". . . the principles of patient protection are an essential basis for the diagnostic applications of radiation, and their adoption should be an integral part of medical, technical, and administrative practice."

But progress cannot stop, accomplishments cannot be erased, the good from radiation still exists. So in controlling and reducing man's exposure from radiation, the government must act in a manner that expands and promotes its beneficial use. This is the challenge that has been thrust on government, individual users, and industry.

Within the Department of Health, Education, and Welfare, the Bureau of Radiological Health is the primary agency concerned with maximizing the beneficial nature of radiation utilization without adverse exposure of man. Many of its activities in the x-ray area are well known. Today we see an example of its efforts in the medical radioactive materials area. This conference, bringing together a group of the leading experts in therapeutic radiation, is looking toward more effective treatment of the patient, including methods and approaches that will encourage dose-reduction for both the patient and medical employee.

Major emphasis by the Bureau of Radiological Health for reducing the radiation exposure of man has been placed on the efficient, safe, and effective utilization of radioactive materials in the healing arts. To effect this goal, Bureau activities have been directed toward both the medical and paramedical community and the agencies regulating radiation use. Program activities may be considered in the context of four broad categories: (1) assessments in problem areas, (2) development of standards and recommendations, (3) development of procedures and methodology, and (4) control program development.

In assessing the extent of the problem of medical radiation exposure and control, various parameters have been investigated.

(1) A contracted survey of the use of radionuclides in medicine by the Stanford Research Institute showed that over 3 million patients received about 5 million radionuclide administrations for diagnosis and treatment of disease in 1966. Of this number, over 111,000 administrations were in the area of brachytherapy, mostly involving the use of radium and radon.

(2) The Bureau's Nuclear Medicine Laboratory in Cincinnati, Ohio, is conducting a continuing program to obtain long-term biological data on radiopharmaceutical behavior, particularly in children.

(3) A survey delineating the gaps and inconsistencies in present State and Federal control of radioactive materials, and recommended needs in this area, was submitted to Congress as a special study under Public Law 90-602.

(4) A State Assignee in Wisconsin conducted a study to assess the magnitude of radiation exposure to medical and paramedical personnel during brachytherapy with radium. Results indicating the need for afterloading to reduce exposure will be presented by Bureau personnel during this conference.

(5) A pilot study of nuclear medicine patient-data reporting has been made, in an effort to develop a system to detail quantities

and reasons for the use of radiopharmaceuticals and procedures in patient populations, as a means of approaching efficacy and overall usage.

In response to the need for uniform guidance at the national level, standards and recommendations have been developed to aid both user and regulatory groups. In addition to reports and journal articles, this has included:

(1) The Bureau-sponsored ANSI Committee N.44 on Equipment and Material for Medical Radiation Applications. (Some of you are probably familiar with the activities of one of the subcommittees interested in therapeutic applications, and their present efforts to develop standards in the area of brachytherapy sources.)

(2) The Bureau sponsored Conference on Reduction of Radiation Exposure in Nuclear Medicine.

(3) Joint participation with the AEC and State radiological health personnel in establishing uniform radiation control activities through the "Suggested State Regulations for Control of Radiation."

To further respond to the goal of reducing exposure in the medical area, various projects have been undertaken to develop methods, procedures, and equipment that would provide useful clinical data with reduced patient exposure, and to examine the use of less hazardous radioactive materials than those presently used. This has resulted in:

(1) The development and promotion of iodine 123 as a substitute for iodine 131 in nuclear medicine by the Nuclear Medicine Laboratory. This more desirable radiopharmaceutical reduces the patient's thyroid dose to about 3 percent of that delivered by iodine 131;

(2) The development of more sensitive nuclear medicine instrumentation and procedures to provide clinically useful data with smaller administered dose;

(3) The feasibility of using low energy seeds for permanent interstitial implants in cancer treatment (contract with Memorial Hospital);

(4) Dosimetric comparison of radium and radium substitutes for medical applications (contract with the 3M Company);

(5) Research and clinical work involving the use of short half-life, low-dose radiopharmaceuticals such as xenon 133 for pulmonary perfusion and ventilation studies, and cesium 129 for cerebral blood

flow and myocardial scanning.

Specific projects have also been carried out to assist regulatory control programs in their radiation activities. These range from evaluation of specific sources or uses of radiation to the development of procedures and methods for program use. Included in these activities are:

(1) A Radioactive Material Reference Manual that provides information on specific sources and devices containing radium, to aid States in their licensing and inspection activities;

(2) The collection and assessment of data in accidents and incidents involving radioactive material sources, to delineate areas in which controls should be strengthened and the type of controls needed;

(3) A radium disposal project that allows States and individual users to dispose of leaking or unwanted radium sources in a safe manner. Testing of many of these sources has been carried out to investigate the physical stresses that cause sources to fail.

This, in brief, summarizes some of the Bureau's activities in the medical radioactive materials area. Much has been done to keep radiation exposure in this area at its present level; however, much remains yet undone to reduce it to the lowest practical level. What is accomplished at this conference will be a step in the right direction. We should all bear in mind -- the government in particular -- that "failure to hit the mark is never the fault of the target."

THE ROLE OF RADIUM AND RADIUM SUBSTITUTES IN THE TREATMENT OF CANCER

John Boland, M.D.

The development of radium in the treatment of cancer began more than 50 years ago, and has matured to stability in the past 10 or 20 years. Radium is suitable for the treatment of accessible cancers, and so carcinoma of the uterine cervix received early attention. More than 50 years ago, Stevenson of Dublin packed hypodermic needles with radium salt for the treatment of cancer in the mouth. He did so at the suggestion of Joly, who pointed out that for even the illumination of a room, multiple sources of light are preferable to a solitary central source.

Regaud of Paris applied radon seeds and radium needles in cancer of the tongue and mouth, establishing a dosage of 1 mCi of radon destroyed per cc of tissue treated, and hence the classical linear intensity of 0.66 mg of radium per cm of radium needle. He also established the standard overall one-week duration for interstitial radiation. Quimby developed a method of dosage calculation for evenly distributed sources. Paterson and Parker developed distribution rules of radium sources for implants of various sizes and shapes, as well as for skin and intraoral molds. These rules are simple enough to enable the physician to plan and execute the implant with a satisfactory distribution of radium.

Paterson's work since 1932 has established that implantation of minimal margins of the order of 1 cm give better results than do larger implantations in tumors of the same size. He also introduced the concept of optimum dose. While a dose of 7,000 rad in 7 days may give an acceptable complication rate, it does not necessarily give the best cure rate; a dose some 5 to 10 percent lower may improve the percentage of cures. Fletcher applied the computer to give detailed isodose distribution around radium implants, conclusively demonstrating that substantial overdosage results in necrosis, whereas substantial underdosage is followed by recurrence.

In radium therapy of cancer of the cervix, Paris, Stockholm, Manchester have all made constributions too well known to be summarized here. The multiplicity of applicators in present day use proves that none is perfect, though many are acceptable. Heyman packing of the uterus with multiple capsules has become standard radiation therapy in carcinoma of the uterine corpus.

Radium is now orthodox treatment for a limited number of cancers. Its use is restricted to cancers that are accessible or can be made accessible by surgical exposure. The most common of these are major tumors of the skin, tumors of the mobile portion of the tongue, and other oral carcinomas. Intracavitary treatment of the corpus and uterine cervix outnumbers all other uses. Smaller tumors of the urinary bladder are also suitable for implantation.

Radium has the great advantage that tumors may be assessed by inspection and palpation, and radium sources introduced with considerable precision. Secondly, since radiation is delivered to a strictly confined volume, the allowable dose is quite high. Thirdly, dose rate can be planned so that the entire treatment is delivered in a relatively short time, usually less than 10 days.

Radium has proved satisfactory for temporary interstitial and intracavitary applications, where it has the great advantage of absolute constancy in dose rate. Radon seeds are suitable for permanent implantation, and some of the newer isotopes offer advantages that have brought them into routine use as radium substitutes. For temporary implantation, the flexibility of tantalum wire and of iridium seed chains proves a considerable advantage in many instances. For permanent implantation, the short-lived isotopes of gold and iodine are satisfactory substitutes for radon seeds. Radium substitutes are particularly suitable in afterloading techniques. This stems from the fact that the sources are physically smaller and more flexible, compared with the rigidity of the radium needle and the relatively large size of the radium tube.

Radium or radium substitute therapy have an assured place in the future. It behooves us to consider what advantages accrue from the use of afterloading techniques.

HAZARDS OF RADIUM AND RADIUM SUBSTITUTES

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RADIUM HAZARDS AND RADIATION EXPOSURE

Gail D. Schmidt, M.S.

Introduction

The subject of radiation hazards from radium is one that has been treated extensively in the literature, particularly as it involves source leakage, facility contamination, and lost radium sources. Through its Radioactive Materials Branch, the Bureau of Radiological Health has maintained an active program in this area, and recently was required by Congress to undertake a special study of the control of health hazards from radium. Section 357a of Public Law 90-602 required the Department of Health, Education, and Welfare to submit to Congress certain studies that included "State and Federal Control of Health Hazards from Radioactive Materials other than Materials Regulated under the Atomic Energy Act of 1954" (1). That report covering radium hazards, characteristics, and uses of medical and nonmedical radium sources and devices, extent and magnitude of use, State and Federal controls, and gaps and inconsistencies in present controls, is used extensively as a resource document for the material presented here. It is also recommended as source for those who desire further references and more detailed information.

In order to place the problems of radium hazards and radiation exposure into perspective, data on the extent and magnitude of medical radium use in the U. S. will be presented.

EXTENT AND MAGNITUDE OF RADIUM USE

Number of Radium Users

The estimated extent and magnitude of the use of radium in the U. S. is summarized in table 1 (1). The number of facilities and the radium inventory in grams has been projected from data covering 13 Agreement States and 7 non-Agreement States.

The 1970 Bureau of Radiological Health inventory of State radiation control agencies reported 2,073 medical facilities licensed or registered as radium users. The actual number of facilities using radium is somewhat higher, since six States reported no medical radium facilities because of a record system that does not provide easy identification of radium users, lack of a program, data not reported, or other reasons. The reported data further indicates that quite possibly 13 States reporting a low number of facilities per million population have not located all users. Accordingly, it is felt that there are at least 2,500 medical radium users -- a figure used later in estimating the number of radium treatments.

Radium Sales

The data on annual sales and leased radium (table 1) was obtained from a questionnaire survey of the manufacturers and distributors. The reports by the manufacturers as well as data gathered in the contract study by Blatz (2) indicate that the sale of medical radium sources has remained fairly constant for several years.

Location

The location of medical radium licenses in Agreement States is indicated in figure 1. These data show the location to be about evenly divided between hospital and private practice locations - and differ with data from non-Agreement States, which show about 75 percent of the radium at the hospital location. The differences are felt to be the result of the regulatory approaches employed.

Source Types

The distribution of the radium inventory by source type is shown in table 2 for certain non-Agreement States. Based upon radioactivity, about 95 percent of the sources are needles, tubes, and cells, with plaques and nasopharyngeal applicators accounting for the remaining 5 percent. As might be expected, clinics and private offices have a higher relative percentage of the plaques and applicators.

Frequency of Radium Treatments

To determine how frequently radium and radon are used in medicine, the Bureau of Radiological Health contracted with the Stanford Research Institute (SRI) to answer this and other questions concerning the magnitude of diagnostic and therapeutic use of radioactive materials in medical practice (3).

The study conducted by SRI consisted primarily of a questionnaire mailed to physicians licensed to possess and use radioactive materials, or registered with State radiological health agencies as possessing such materials. The names and addresses were obtained from the Atomic Energy Commission and State agencies.

Based on the data obtained, it can be estimated that in 1966 (when the study was conducted) approximately 85,000 radium and radon treatments were provided to 61,500 patients. That estimate, projected on the basis of 2,500 radium facilities, is summarized in table 3 by treatment group. This value is 2-1/2 times greater than the 33,310 brachytherapy treatments using byproduct materials during the same period. The majority of byproduct treatments were treatments of the eye using strontium 90 plaques (table 3).

RADIUM HAZARD STUDIES

State Inspection Findings

As States became involved in the control of radium, initial emphasis was placed on its use in medical facilities. This area was chosen because:

1. Users would be members of the healing arts who already were licensed for the practice of medicine by the State. Hence a potential listing of the users was available, and through questionnaires their possession or use of radium could be determined;

2. The largest amount of radium was thought to be used by the medical profession;

3. Medical use most likely represented the largest potential for radiation exposure of individuals.

Some of the initial findings of such surveys up through the mid-sixties are shown in table 4. This table gives some indication of conditions existing prior to any attempt at regulatory control, and the extent of conditions requiring corrective action. It is probably representative of conditions in most States prior to an active regulatory program. Findings from the Wisconsin study of 1968-1970 (table 4) should not be considered an initial survey, since 28 (35 percent) of the facilities had been surveyed earlier. It should also be noted that 41 facilities (51 percent) lease radium on a per case basis, and did not have radium at the facility when surveyed (4).

Inadequate source storage indicates a potential for exposure of physicians, other staff personnel, and members of the general public. For example, a facility in Chicago had such inadequate storage that the dose rate in an insurance office on the floor above was approximately 10 times the maximum permissible level (12). However, adequacy of source storage is only one item in a facilities radiation protection program. Unnecessary exposures can occur when applicators are loaded or unloaded during transport to and from treatment areas, during applicator or source insertion, and during patient irradiation. Control of exposure depends on precautions taken by the responsible individual to maintain exposure as low as practicable.

The posting of radiation areas and labeling of radiation sources are important considerations in the safe handling of radioactive materials. Without indication that radiation sources are present, unaware individuals may inadvertently be exposed to unnecessary radiation. Furthermore, sources have been lost because an individual removed or disposed of unlabeled containers.

A problem of greater occurrence with far reaching implications is the integrity of radium sources. The initial surveys indicated that 13 to 50 percent of the facilities had leaking or contaminated sources. The leakage serves to indicate that the source encapsulation may be weakened, which could result in rupture of the source. The inadvisability of using leaking or contaminated sources in patients is obvious. Equally obvious is that leaking sources could lead to contamination of facilities, and this in turn could lead to contamination of people.

Decontamination cost for medical facilities has ranged as high as $50,000 (13). An industrial facility contaminated with radium necessitated vacating and loss of a building valued at approximately $250,000 (13). Not included in this cost is the time expended by State and Federal personnel in decontamination activities, nor the resulting loss of income by physicians or industry while the facility is undergoing decontamination.

Radium Incidents

Since 1962, the Bureau of Radiological Health of the Public Health Service has collected, analyzed, and disseminated radium-incident information (14,15). The objectives of this program are to provide information with regard to:

1. Extent of radium incidents
2. Causes
3. Design of preventive measures
4. Trends in the occurrence of incidents

For our purposes, we have defined an incident as any loss, theft, contamination, overexposure, or other extraordinary occurrence. Reports of both past and current incidents are collected from a variety of sources. At present State health agencies are the primary sources of information, but in the past many accounts of incidents were provided by a newspaper clipping service, the literature, and reports from persons intimately associated with the use and production of radium.

Starting in about 1966, reports of incidents involving special nuclear material, byproducts and source material have been collected for study. (Hereafter they are referred to as byproduct incidents.) These incidents have largely been collected from the AEC's Exchange of Information Calendar and, of course, again from State health agencies. The reports have not been analyzed in detail; however, information on 303 in the period from 1966 to 1969 is presented here.

The bottom curve of figure 2 shows the number of radium incidents used for our analysis. Occurring at a basically constant rate since 1964, they average about 28 per year. The byproduct incidents currently average about 75 per year. The number of incidents involving radium is about 40 percent of the byproduct type. On the basis of the relative number of type facilities, radium incidents represent about 35 percent higher rate of occurrence (estimate of approximately 4,200 radium facilities versus 15,000 AEC and State byproduct licenses).

Figure 3 compares byproduct and radium incidents by type; that is, loss, theft, contamination, overexposure, and miscellaneous. It will be observed that losses are the most prevalent, with byproduct overexposures of almost equal magnitude, and contamination incidents third in importance. This relative prevalence of incidents is probably characteristic of the type of sources in use -- small radium brachytherapy sources versus many large byproduct sources for radiography and irradiation. Apparently the greater activity accounts for the high prevalence of overexposure in byproduct incidents.

It is interesting to note that of the medical incidents 81 percent are radium, only 10 percent involve byproduct materials. On this basis, during the period 1966 to 1969 there were 41 radium incidents per thousand medical facilities as opposed to 5.3 byproduct incidents per thousand medical licenses, representing a significantly higher rate of occurrence for radium.

Since 72 percent of the medical radium incidents were losses, these are examined in figure 4 with regard to the point at which the loss occurred. Predominantly, it occurred during treatment and removal, particularly when the source became dislodged and was discarded by the patient, when the source was discarded with gauze packing and disposable applicators, or during similar situations -- for example, source falling on the floor and being swept up by the cleaning staff.

When incident data for the period 1966 to 1969 are compared to those prior to 1966, they show no significant change in percentage of occurrence during treatment and removal. Losses during treatment have increased from 27 to 36 percent in the 1966-1969 period, while losses during removal have remained constant.

Other characteristics of radium incidents from the paper by Villforth et al.(16) are given in table 5. They show that lost radium generally is recovered from the trash or disposal system, and that 59 percent of source ruptures are due to an externally applied force.

PERSONNEL EXPOSURE STUDIES

While a considerable number of papers have been written on the subject of radium hazards, there is a paucity of information on the occupational exposure of medical staff participating in brachytherapy. Radiation exposure is of particular significance to this conference, since afterloading can and should result in considerable reduction of exposure. Unfortunately, exposure studies utilizing afterloading were not found in the literature for comparison with exposure data involving preloaded applicators.

One of the most comprehensive (and recent) studies of occupational exposure during brachytherapy was performed by the Wisconsin Division of Health as part of a State survey of radium facilities reported on earlier in this paper (4). The Wisconsin studies emphasized two aspects: (1) the necessity of extremity monitoring for individuals who load applicators; and (2) the monitoring of medical personnel for one calendar quarter, to determine the magnitude of personnel dose.

Exposure During Applicator Manipulations

In order to collect extremity dose information, the Wisconsin Division of Health provided personnel dosimeters to individuals who loaded, unloaded, inserted, or removed radium applicators. The extremity dosimeters were TLD rods sealed in plastic tubing and supplied by the Bureau of Radiological Health. To obtain comprehensive dose data, the following sites were monitored: right index finger, right wrist, left index finger, eyes, and torso. In addition, a film badge was also used to monitor the torso.

Table 6 is a summary of the monitoring results for 10 different participants at eight installations. The dose is expressed in mrems per 100 mg of radium manipulated, where milligrams loaded and unloaded are added separately. As would be expected, doses to various body sites show considerable variation. With regard to the requirement for extremity monitoring, it may be observed that extremity doses for all L-block users exceeded eye and body doses by a factor greater than 15, which is the ratio of recommended annual dose limits. The area of high extremity doses were quite limited, however; there, wrist doses were only a factor of 3 greater than eye and body doses.

The data in table 6 also clearly show that the radiation protection afforded by L-block use results in eye and body doses lower by factors of 5 and 3, respectively. Some of the ambiguities in table 6, such as the L-block affording protection for the wrist and greater protection for the eyes than the body, are not clearly understood. It is felt, however, that these variations result from the limited amount of radium manipulated in some categories, and that individual variations are important. In this regard, it should be noted that one individual manipulated all the radium involving the Ernst applicator, and his doses have a strong influence on the average data for all L-block users.

It is felt that one would expect different doses during the loading of applicators of differing complexity. However, the data again probably reflect individual variation in technique, particularly with regard to the low eye dose for the Ernst applicator.

The extremity doses found in the Wisconsin study compare favorably with similar studies reported in the literature. When the data are normalized for comparison, the average right index finger dose is 470 mrems per 1,000 mg-min in the Wisconsin study, compared to a value of 360 mrems/1,000 mg-min reported by Robb and Ellis (17) using film, and 710 mrem/1,000 mg-min by Howarth et al.(18) using small ionization chambers.

Exposure of the Hospital Staff

In order to determine the necessity for routine monitoring of hospital staff, the Wisconsin Division of Health assisted 20 installations by providing film badges to monitor the staff for 3 consecutive months (4). During this period, approximately 300 individuals were monitored for whole-body doses at 18 facilities, and 221 individuals received doses greater than 10 mrem (the lower detection limit of the film badge). This exposure was accumulated during 37 brachytherapy treatments of unspecified type (the majority were probably intracavitary treatments).

The results of this monitoring of the hospital staff engaged in radium brachytherapy treatments are summarized by job position in table 7. The physician category was found to average more than twice the exposure of any other group. It was noted, however, that a large portion of this total was received by 3 physicians with doses of 600, 1,240 and 1,360 mrems. Similarly, 2 nurses had doses of 1,130 and 1,220 mrems. When these data are omitted, average doses to physicians are 72 mrems, to nurses and aides 59 mrems. When the categories of nurse and aide are examined separately (eliminating the data for females of unspecified job position), average doses are 92 and 55 mrems to aides and nurses, respectively.

Data reported by Eastern Germany in a preliminary UNSCEAR report gave a value of 0.79 rems/year for medical radium workers. In a study of radiation levels surrounding patients treated with 100 mg of radium for cancer of the cervix, C. E. Nurnberger (19) noted levels of 100 mr/hr in the region where nurses and aides provide bedside care. This compares well with the dose to aides of 92 mrem, since the average reported exposure time was just over 1 hour.

There were several indications that the exposure to hospital staff in the Wisconsin study should be considered minimum. These include:

(1) Although the average physician dose was 172 mrem (or 72 mrem when the 3 high exposures are included), no physician doses were recorded for 14 of the 37 treatments. There was no indication that any of the monitored physicians utilized afterloading.

(2) Although an average of 7 individuals recorded doses per treatment during 10 treatments (27 percent), only 4 individuals recorded doses greater than 10 mrem. This suggests that the wearing of personnel monitoring badges may not have been very complete.

(3) After completion of the study, the film badges used in the study were exposed to known radium doses. Three badges exposed to 30 mrems all reported less than 10 mrem. While the film badge results were low for the next higher dose (350 mrems) and above, the deviations were less than 10 percent.

The following observations and conclusions can be drawn from this study:

(1) The dose to nurses and aides is essentially equal to that of physicians.

(2) There is an indication that of all hospital personnel, the aides receive the greatest dose, apparently because their duties involve direct bedside care of the patient.

(3) As a group, nurses and aides receive 69 percent of the total staff dose during brachytherapy.

(4) The total dose of 18,170 mrems during 37 treatments indicate a total dose per treatment of about 0.5 man-rem.

(5) Based on the SRI data (table 3) indicating about 60,000 intracavitary and interstitial treatments per year, the annual dose to personnel in all facilities in the United States is a minimum of 30,000 man-rem.

(6) Based on quarterly monitoring showing 11 individuals exposed at each facility, the average annual doses may be about 1 rem per individual.

SUMMARY

Radium is being used today in approximately 2,500 medical facilities to provide about 85,000 brachytherapy treatments per year. Although the use of byproduct materials (and others) has found acceptance for brachytherapy treatments, the sale and lease of radium continues at an undiminished rate.

Data from initial State surveys of these facilities indicate a relatively low degree of compliance with the provisions of State radiation protection regulations. Although current data is not available from an adequate sampling of States, it is the author's opinion that compliance with radiation protection recommendations today is generally inadequate (4). These inadequacies result in high rate of radium incidents (lost medical sources), use of leaking sources, and generally high levels of personnel exposure.

The Wisconsin survey indicated that only 50 percent of the facilities provided personnel monitoring to brachytherapy users, and then frequently to only one individual (4). Data on radiation exposure did not indicate that any large number of individuals would exceed the occupational limit of 5 rems per year. Exposure of the hospital staff is, however, relatively great on both an individual and total man-rem basis, when compared to other occupational groups.

Preliminary estimates by the Bureau of Radiological Health indicate that total exposure to the 360,000 x-ray operators may range from 32,000 to 113,000 man-rems. Similar estimates for industrial radiographers, who are considered a high exposure group, indicate a total dose of 10,000 man-rems.

It should also be noted that the most recent recommendations of NCRP (20) include in the category of "occasionally exposed individuals" maintenance workers, nurses, hospital visitors, etc. The exposure of the occasionally exposed should be limited to one-tenth of the occupational limits, or 500 mrem per year. In exchange for more restricted control of personnel exposure, the controlling organization has a reduced (or even no further) obligation to assure that the exposed individual is knowledgeable concerning radiation protection practices.

These recommendations appear to be appropriate for the brachytherapy exposure situation observed during the Wisconsin study. The facilities surveyed reported an average radium use of about one treatment per month, and those facilities where personnel monitoring was conducted apparently had an even lower frequency of use. However, the radiation protection officer at these facilities had minimal training, and almost no effort was made to control or monitor exposure of the hospital staff

The adoption of afterloading (both simple and remote) is one positive way to ameliorate the inadequate radiation protection practices associated with brachytherapy. For instance, by eliminating radiation from the operating room simple afterloading may reduce total radiation exposure to the staff by 25 to 50 percent. And high intensity remote afterloading in a shielded room should eliminate essentially all exposure to the hospital staff. It is also felt that adoption of remote afterloading, perhaps restricted to the larger hospital, would result in improvement of all radiation protection practices.

While reduction of radiation exposure is important, the primary concern must be more effective treatment of the patient. If afterloading does result in more effective treatment, then radiation protection aspects are added justification for the adoption of afterloading.

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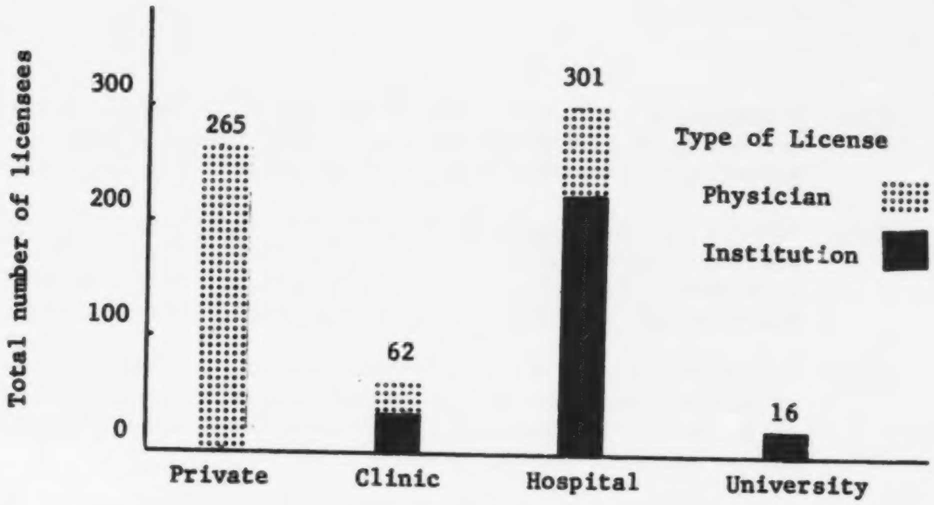

Figure 1. Location of medical radium licensees in 16 AEC agreement states.

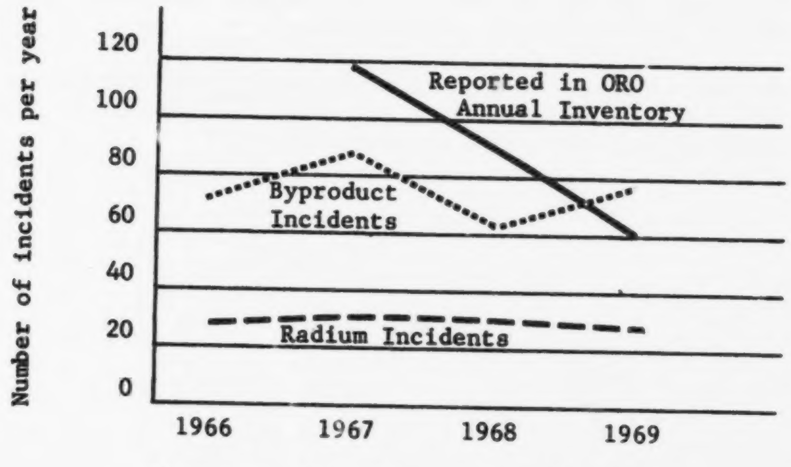

Figure 2. Annual rate of radioactive material incidents.

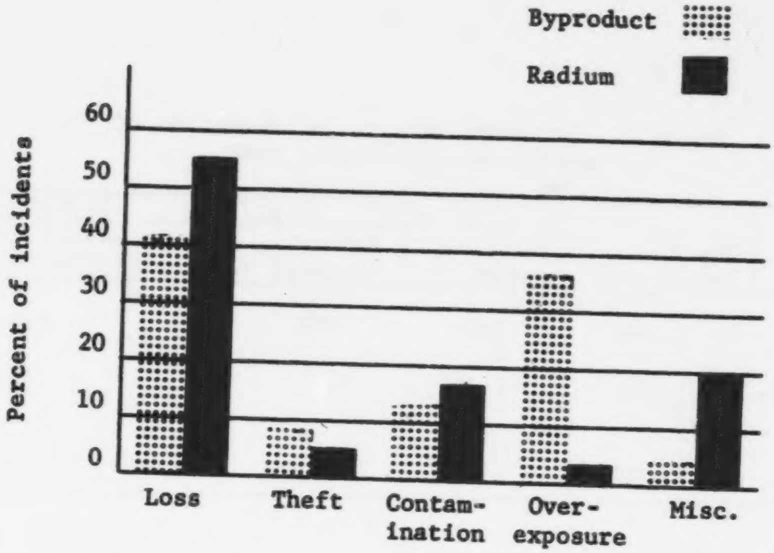

Figure 3. Type of byproduct and radium incidents 1966-1969.

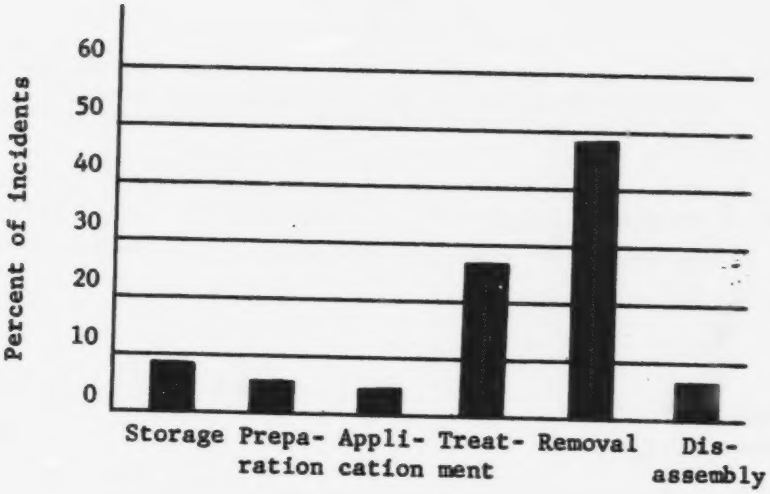

Figure 4. Point of medical radium losses, all data (Total Incidents - 162).

Table 1. Estimated extent and magnitude of radium use and sales, 1968

Type of use	No. of facilities[a]	Annual Sales 1967-68 Inventory (grams)[b]	Annual Sales 1967-68 Radium (grams)	Annual Sales 1967-68 Radon (curies)	Leased radium 1967-68 (grams)
Medical	2,280	326	3.04	21	103
Nonmedical	1,850	148	7.5		49
Total	4,130	474	10.54	21	152

[a] Excludes Federal use

[b] Includes leased radium

Table 2. Distribution[a] of medical radium sources by type of source in certain non-Agreement States[b]

Type of sources	Hospitals (percent)	Clinics and private offices (percent)	Total (percent)
Needles, tubes, and cells	85.7	8.8	94.5
Plaques	0.6	0.7	1.3
Nasopharyngeal applicators	1.2	3.0	4.2
TOTAL	87.5	12.5	100.0

[a] Distribution based on the activity of sources in curies

[b] Representing a population of 38.5 million

Table 3. Projected annual brachytherapy treatments in the U. S. - 1966

Treatment type	Projected annual treatments - 1966	
	Radium	Radium substitutes
Intracavitary	42,400	6.080
Interstitial (Temporary)	11,200	[a]1,760
Interstitial (Permanent)	8,300	200
Ophthalmic	270	21,800
Dermatological	15,100	2,200
Nasopharyngeal	7,700	1,260
TOTAL	[b]84,970	33,300

[a] Iridium 192 used interstitially assumed to be a temporary implant

[b] For 2,500 facilities - average of 34 treatments/facility

Table 4. Summary of State initial radium survey results

State	Hazardous conditions found			
	Inadequate source storage (percent)	Improper or no labelling (percent)	Leaking or contaminated sources (percent	Contamination or decontamination required (percent)
Kansas (5)	30	95	50	--
Pennsylvania (6)	44	100	46	--
Alabama[a] (7)	--	--	40	40
Alabama (8)	--	--	43	20
Minnesota (9)	21	--	37	79
Kentucky (10)	10	35	35	--
Georgia (11)	37	87	53	51
New York[b] (13)	20	--	27	--
Indiana (13)	23	--	13	--
Wisconsin '68-70 (4)	13	13	46[c]	--

[a] Jefferson County only

[b] Excluding New York City

[c] Percentage of 39 facilities that own radium; no per case leased sources are included

Table 5. Other attributes of radium incidents

	(percent)
Recovery of lost or stolen radium (299)	66
Recovery site of medical radium losses (171)	
Trash system	54
Sewerage system	11
Floor of facility	11
Other	24
Causes of radium source rupture (48)	
Internal pressure (spontaneous and heat)	14
Crushed	10
Tip broken or pulled out	36
Drilled or cut	13
Other or unknown	27

Table 6. Summary of extremity and body doses during the manipulation of radium sources

Applicator and use condition	Dose (mrem/100 mg)			
	Right index finger	Right wrist	Eyes	Body badge
Load and unload with L-block				
Heyman (980 mg)	84	14	8	6
Tandem (470 mg)	104	44	23	12
Ernst (2,320 mg)	230	29	4	11
Needles[a] (68 mg)	490	194	170	85
L-block operations				
(3,640 mg)	182	27	8	10
Non-L-block operations[b]				
(300 mg)	174	59	43	31
Insert and remove				
Tandem (220 mg)	87	22	8	13

[a] Partially no L-block

[b] Involved 8 percent of all load and unload operations on a milligram basis

Table 7. Dose by job position

Job position	Number of individuals	Percent	Total dose accumulated (mrems)	Average dose/ individual (mrems)	Range of individual doses/quarter[a] (mrems)
Physician	30	14	5,150	172	20-1,360
Nurse,aides[b]	174	78	12,490	72	10-1,220
Other	17	8	530	31	10-120
Total	221	100	18,170		
Overall				82	10-1,360

[a] A calendar quarter was the maximum interval. Some individuals were monitored for one month or treatment then rotated to a different department of the hospital.

[b] When not specified, females were assumed to be nurses or aides.

RADIUM AS A PROBLEM BYPRODUCT OF URANIUM

John H. Harley, Ph.D.

You have heard about some of the problems that occur in the medical uses of radium. I might add in this context that the Southeastern Radiological Health Laboratory, which is now under the Environmental Protection Administration, estimates that about 2,000 grams of radium 226 have been processed and imported for use in medical and industrial sources. They can account for about 700 grams of this material, and we can only assume that the rest is lost, strayed, or stolen. This problem antedates the age of uranium processing, and I am not going to count it in my total.

The thought of 2,000 grams of radium is rather staggering in itself. It does not seem as high if you consider that the 1969 production of uranium oxide was about 10,000 tons. I would estimate that in bringing this amount of uranium to the surface they also brought about 1,000 grams of radium with it. If you remember that uranium production and processing has been carried out on a large scale for the past 25 years, you can see that a considerable amount of radium has been brought into our environment.

In the early days of the Manhattan Project and Atomic Energy Commission, the uranium ores came from the Belgian Congo and there was agreement that the radium remain the property of the ore supplier. The U. S. Government separated and stored this radium in the form of sludges and other residues. At the present time several hundred grams are stored, and it seems unlikely that the original supplier wants it back. This material is one obvious radium problem.

When emphasis on uranium procurement shifted to the U. S., the Atomic Energy Commission began to purchase uranium oxide concentrates rather than ores. The mining and milling of uranium ores were in the hands of commercial companies with long histories of experience with other materials. Radium was a byproduct and appeared in the materials known as tailings, which gradually accumulated around the uranium mills. The concentration of uranium in the local ores was not as high as those from the Congo, thus the radium concentration in the tailings was not high. On the other hand, gamma radiation levels on the piles were up to 1 mrad/hr and they continually emanated radon into the atmosphere. These tailing piles are the second problem with byproduct radium.

The actual gamma levels were not too important, because no one expected that anyone would live or even work on the tailings piles. On the other hand, the radium did begin to disperse into the environment. In one case it contaminated the Animas River in Colorado to levels that were well above those considered permissible for drinking water. The runoff from that particular tailings pile was controlled, and attention was given to stabilizing other piles so they could not contribute to ground water contamination.

The emanation of radon from the piles did give excessive air concentrations of up to 30 pCi/l on the pile itself, but dispersion of radon and its daughters did not lead to measurably elevated levels in populated areas. It appeared that perhaps the problem of tailings piles was under control.

About 5 years ago a number of people began to consider the fact that the coarse tailings, which resemble sand, had been used as a source of fill and even building materials. This was first brought to public attention in Colorado, and in 1966 that State ordered the practice stopped. Measurements made in a few houses and other buildings in the area of Grand Junction, Colo. showed that measurably high levels of radon existed in a number of buildings. State and local health officials began the job of tracking down where tailings had been used, and found that a large number of houses had used these sands under concrete slabs and around their foundations. The material had also been used under streets and driveways, and as fill around water pipes and sewer mains.

The next step was a survey of houses in the Grand Junction area. Out of about 5,000 homes or additions checked up to the first of this year, about 50 percent were found to have tailings on the property. This is the third problem of byproduct radium.

At the request of the Colorado State Department of Health, the Surgeon General set the following levels for exposure in these homes:

External Gamma Radiation	Recommendations
Greater than 0.1 mR/hr	Remedial action indicated
From 0.05 to 0.1 mR/hr	Remedial action may be suggested
Less than 0.05 mR/hr	No action indicated

Indoor Radon Daughter Products	Recommendations
Greater than 0.05 WL[1]	Remedial action indicated
From 0.01 to 0.05 WL	Remedial action may be suggested
Less than 0.01 WL	No action indicated

[1] Working Level - Unit of radon daughter product exposure for miners

For comparison, the external gamma radiation in houses in New York City might be about 0.01 mR/hr, and the radon daughter levels about 0.002 WL.

Measurements are now continuing, and it is apparent that a large fraction of the houses with tailings fall into the group where remedial action is indicated. The actual remedial action that will take place might well be considered as our fourth problem with radium as a byproduct of uranium.

RADIUM LEAKAGE

Hanson Blatz, E.E., P.E., FACR (Physics)

The new York City Office of Radiation Control of the Department of Health was established 12 years ago to institute a program designed to protect those using radiation emitters such as radioactive materials, x-ray machines, and other sources against excessive or unnecessary exposure to ionizing radiation. The program also is concerned with the protection of medical patients and other persons in the vicinity of radiation sources. Physicians, scientists, and technicians are encouraged, and in some cases required, to follow certain generally accepted practices based primarily on recommendations of the National Council on Radiation Protection and Measurements. An effort is made to update the regulations as new information is gained from radiation exposure experience.

All radioactive sources used in medicine, education, and nonprofit research come under the jurisdiction of our Radioactive Materials Division, which licenses radioactive materials and makes periodic inspections required under an agreement with the U. S. Atomic Energy Commission. The program also covers radioactive materials such as radium not normally under the jurisdiction of the AEC.

During the past decade, there have been many references in the literature to the fact that radium is one of the more hazardous radioactive materials in use, and many people have urged that efforts be made to replace it with other radioisotopes. There have been several references in the literature to encapsulated radium broken open as a result of accidents. A few of the older radium needles were reported to have exploded for reasons that have not been completely clear. There have been many references to leaking radium, and methods for testing for leakage.

In an attempt to determine whether to adopt a policy of either encouraging or requiring replacement of radium by less hazardous radioactive materials, the literature was searched for evidence of exposure risks to users as a result of the reported accidents. Considering the large quantities and widespread use of radium in the past 75 years, very few cases of radium leakage have been reported. Except for a few cases of gross mishandling, no evidence could be found of an accident resulting in the release of the radium salt itself from the encapsulation during the past 40 years. Typical examples include one in 1955 in which radium needles were sterilized by boiling them in a dish of water. The water was allowed to boil dry, the solder used to seal the needles apparently melted, and the point of one needle fell off. In another case, a lead transport container fell off a cart and dropped to the floor, distorting the lead shielding plug so that it could not be removed. In drilling through the plug, the radium inside was damaged and some of the radium was released. In no such accidents was exposure of persons to contamination in hazardous amounts reported.

It would appear then that except for a few accidents, the principal problem is leakage of radon gas through minute pinholes in the encapsulation seals which do not permit release of the radium salt itself. This means that the primary source of contamination hazard to users would probably be inhalation of radon gas and airborne radon decay products.

Because there appeared to be considerable difference of opinion regarding the magnitude of any hazards associated with leaking radium applicators, the Bureau of Radiological Health of the U. S. Public Health Service was approached with a proposal that investigation be made of all the radium used medically in New York City. From registration figures it was estimated that more than 20 curies of radium was in the hands of medical users, in about 3,000 needles and tubes and a few beta-ray applicators, at 99 different hospitals and physicians' offices.

There has been concern about the health hazards associated with radium for many years. As early as 1932, there were reports of a high incidence of lung cancer among Southeast European miners. These were based on studies of the incidence of lung cancer among miners and of radon concentrations in the mines. In the early 1930s, the U. S. Advisory Committee on X-Ray and Radium Protection issued recommendations to reduce human exposure. These were contained in National Bureau of Standards Handbook 18 entitled "Radium Handling," and were concerned only with external gamma radiation exposure. A subsequent Handbook H-23 issued in 1938 also dealt primarily with external gamma exposure, although it did mention that the danger of radon inhalation should be avoided by ventilation, and suggested 8 changes of air per hour in all workrooms. The first mention of a numerical concentration limit was in a 1941 Handbook 27 entitled, "The Safe Handling of Radioactive Luminous Compound," but these recommendations applied to places where unsealed radium was openly used.

It is interesting to note that the recommended figures at that time do not differ significantly from those considered satisfactory today. It is expected that numerical values were not suggested until then because of the inability to sample and measure radon concentrations satisfactorily. From that time on, there have been a series of handbooks issued by the Advisory Committee that subsequently became the National Committee on Radiation Protection, and more recently the National Council on Radiation Protection and Measurements. These were issued in 1942 (H-38), 1949 (H-42), 1950 (H-47), 1951 (H-48), 1953 (H-52), 1954 (H-54), 1959 (H-69), and most recently in 1960 (H-73), totalling 11 in all.

Although in the 1954 report there was casual mention of loss of radium resulting from accidents, there was no mention of radon leakage or testing until the 1960 report, which recommended a test for contamination prior to release by the manufacturer and periodic leak tests during use. The recommendation is for a leak test at least every 6 months, except for solid corrosion-resistant metal or alloy sources. The sensitivity of the test is described, but no clear indication is made of what degree of contamination constitutes a hazard.

After serious consideration of the advantages of a 6-month leak test, offset by the additional gamma radiation exposure incurred by those who must conduct the test, the New York City Health Department compromised with a requirement for an annual leak test. Even this requirement was not vigorously enforced because of considerable uncertainty about the need for such tests, combined with the quite evident fact that some of the leak testing of thousands of sources must be done by individuals who have not had special training and are not particularly qualified to conduct such tests.

Growing evidence that the leakage of radon -- were it to occur -- does not constitute a significant hazard led to proposal of a comprehensive radium leakage study.

In reviewing the literature, and corresponding with those involved in reported contamination accidents, it appeared that there was no particular concern about leaking sealed sources of radioactive material until about 1957, when two accidents occurred -- one at the Oak Ridge National Laboratory Hospital and the other in Massachusetts. In both cases, substantial leakage of cobalt 60 dust was detected from cobalt teletherapy sources. It appeared that the intense gamma radiation had a destructive effect on lead washers used to seal the screwcap on the source capsule. Although the two incidents were considered serious in terms of released radioactive contamination, investigation revealed no evidence that anyone had been overexposed, nor that there was detectable uptake in the bodies of the individuals involved. After these two incidents, however, there was active promotion of periodic contamination testing of sealed sources.

The special case of the beta-ray plaques should be mentioned in passing. About 1910, dermatologists discovered that radium salts with a minimum of filtration emitted potent beta radiation that could be useful in treating certain skin disorders. The first applicators were made by applying the radium salt to a flat surface and covering it with a thin coat of varnish. Later, about 1920, the method of securing the radium was improved by mixing it with a ceramic powder and then firing the mixture until it became glazed. This was an improvement, but it was found that the slightest mishandling resulted in the brittle ceramic surface chipping or powdering off, causing loss of some of the radium. Finally, in the mid-30s the radium salt was covered by a very thin (0.1 mm) monel cover sheet that has proven more satisfactory, though surface contamination sometimes can be detected on the monel.

The radium contamination study was initiated in July, 1966, and it was found that a total of 21,580 mg of radium for medical use had been registered with the New York City Department of Health. The radium was distributed among 2,957 separate sources in 56 hospitals and 43 physicians' offices. During the course of the investigation 1,811 mg of radium not previously registered was found, often because the owners (particularly large hospitals) were not certain about the total amount of radium in their possession until careful inventory was taken. It should be noted that as a result of the study almost 200 mg of radium was disposed of, either because it was leaking and the owners did not consider it worth the expense to have it repaired, or it had not been used in years and its maintenance was a nuisance. Many now prefer to rent the radium as needed.

The first problem was to decide upon a satisfactory leak test method. The literature contains many different methods for leak testing radium. A particular advantage is claimed for each. Because of the large number of sources to be tested, we needed a method that was relatively simple, quick, reliable, and reproducible. Such a system, to be satisfactory for this large scale study, must be easily performed by relatively untrained persons after their instruction, and should not result in the technician receiving significant amounts of radiation exposure; in other words, the sampling should be quickly performed with a minimum of radium handling. It was evident that the entire stock of radium sould not be taken out of service at one time for the purpose of repeated leak testing. It also is impractical to take sufficiently sensitive instruments in the field for accurate leak test measurements. Transportation of 3,000 radium sources to a central laboratory for testing was out of the question. For these reasons, a mail-order method is preferable. It was learned that the Radium Chemical Company has been conducting for many years a mail-order leak-testing service that has proven quite satisfactory. Through cooperation of that company, our staff was thoroughly indoctrinated in the test methods and necessary equipment.

The method chosen consists of placing the needles to be tested (usually 9 or less) in a small plastic vial containing water and a small amount of versene. The applicators are left in the solution for 24 hours in a secure place, then removed from the vial. A screw-cap is placed tightly on the top of the vial containing the solution, it is placed in a special mailing carton and mailed to the Office of Radiation Control Laboratory. There the vial containing the solution is placed in a well counter, where the presence of any contamination is detected and measured.

During this time, the applicators that have been tested must be segregated, so that the test can be repeated if contamination is found. It often occurs that an applicator or group of applicators found contaminated apparently have been cross-contaminated from another leaking source, since the repeat test shows little or no contamination. The contamination evidently washed off during immersion in the versene solution.

When a group of applicators shows significant contamination on repeat test, it is evident that at least one is leaking. In that case, each one is tested separately, the leaking applicator or applicators are identified and taken out of stock for repair or disposal.

Another aspect of the study was to make measurements of airborne radon gas concentrations at places where radium is stored or prepared. Although many measurements were made in hospitals and in physicians' offices, the only places where radon concentrations approached the maximum permissible limits were radium storage rooms that had been closed for some time. In such cases it was invariably found that after the door had been open a short time, natural ventilation reduced the concentrations to the point that they were insignificant. This was observed even in locations where considerable radium leakage later was found.

One of the primary objectives of this study has been an attempt to detect the effect of radon leakage exposure on persons working with leaking sources. After investigating several possible methods of examining exposed persons, it was decided to conduct urinalysis for lead 210.

A simplified method for determining radon decay-product body-burden by urinalysis for lead 210 content has been developed at the New York University Institute of Environmental Medicine, in connection with a study of uranium miners exposure to radon and radon decay products. During the course of that study, 15 individuals were selected for urinalysis either because they had worked with leaking radium sources or had worked for long periods of time during which sources presumably handled by them were known to be leaking. It is interesting to note that none of the persons selected as most likely to have been exposed to radon decay products, in this large population of radium handlers, showed any evidence of lead 210 in excess of normal background. Admittedly this is not a particularly sensitive method, but it has proven capable of showing significant exposure.

The common apprehension about ingestion of contaminants has been thoroughly investigated over the years. It has been amply demonstrated that transfer of surface contamination by hands, eating, smoking, applying lipstick, etc. is an extremely inefficient way of introducing contaminants into the body. It is true that radon gas in the environment can deposit solid decay products anywhere. Surface wipe test showed that contaminated surfaces were limited to work surfaces, storage containers, and tools that come into direct contact with the radium applicators. Since workers are not expected to hold radium in their hands, the chance of ingesting contamination is nil.

Another question has been raised about needles and tubes from which radon gas is leaking, and the extent to which patients could become contaminated when the radium is applied interstitially or in body cavities. A review of methods of sterilizing radium before use, and the practice of further enclosing tubes in applicators when placed in cavities, both would tend to reduce any risk. There is evidence that freshly-cleaned leaking radium builds up surface contamination at the rate of thousandths of microcuries per day. This would indicate that contamination would be insignificant even in case of insertion of a bare leaking needle, and would decay rapidly upon removal of the needle.

Our conclusion, therefore, is that a radium applicator does not constitute a significant health hazard either to users or to patients, even when it is leaking radon, unless it is damaged to the extent that the radium salt spills out, which can most likely be observed by inspection.

This then raises the question whether periodic leak tests are justified, when balanced against external gamma exposure to the person doing the testing. Radium needles and tubes should be examined carefully for evidence of damage or faulty soldered joints whenever they are used, and then tested if necessary, even though recently leak tested.

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PRESENT POSITION OF BRACHYTHERAPY - METHODS AND MATERIALS

Margaret D. Snelling, F.R.C.P., F.R.C.S., F.F.R.

Teletherapy has developed enormously over the past 25 years and recent technological advances now make it possible to review and develop the techniques and possibilities of brachytherapy.

In teletherapy, the combination of meticulously observed clinical radiotherapy with the precision of treatment dosimetry has provided techniques by which we can deliver any required amount of radiation to every selected volume of the body - with treatments given usually at a rate of 1-2,000 rads per week at dose rates of a few hundred rads per minute. Planned multifield deep x-ray treatments were succeeded by rotation therapy with more elegant work for the physicist, while for a time grid techniques with their mixture of radiobiological fantasy and clinical efficiency gave surprisingly good palliative results. Many of the patients still survive to surprise us. The development of radiocobalt kilocurie units, with their increased energy and high dose rates, revolutionized treatment by making possible precise, and simple, and easily repeatable techniques for the treatment of tumors in all parts of the body. In the United Kingdom, high energy betatrons with x and beta rays have not been thought to offer important radiobiological or dosimetric advantages, but 4 to 8 MeV linear accelerators are increasingly used for treatment of the majority of deep seated tumors, and for treatment of more superficial tumors (such as carcinoma of the ethmoid), where precise dosimetry is essential to spare adjacent structures.

By the use of beam direction, tissue substitutes, compensators, wedges, and so on, the required dosimetry can be produced in any part of the body, while the lower energy electron therapy provided by some linear accelerators offers an alternative method for the treatment of superficial tissues.

In spite of these advances in technique, failure rate remains high. Further improvement of results depends on many factors, including advances in dosimetry made possible by the computer, and modification of chemotherapy, and immunotherapy.

Other changes in technique depend upon our increased understanding of efforts of radiation of the cell.

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The solid growing tumors with long natural histories - for instance, carcinomas arising in breast, nose, throat, and uterus produce special problems. Here, spread is relatively late and failure is associated almost invariably with local residual disease. Study of these poorly vascularized tumors in the light of modern radiobiological concepts has resulted in attempts to improve the effect of radiation on hypoxic cells by sensitization in the hyperbaric oxygen chamber, and by the reintroduction of neutron therapy.

Studies of cell kinetics have also led to a review of dosage and fractionation studies made by the pioneers in radiotherapy, and to a renewal of clinical interest in the relationship between dose rate and response of hypoxic tumors to irradiation. There are some theoretical grounds for believing that these slowly growing tumors will respond better to continuous low dose rate therapy than to such fractionated high dose rate treatment as is given by supervoltage x-ray and kilocurie apparatus. Since many of these tumors are either relatively superficial, or at least are accessible through the body cavities, we have been led to a review and to the further development of brachyradiotherapy - techniques long ago established in the treatment of accessible cancer but in recent years regarded with less favor because of the inevitable associated irradiation of personnel.

With the introduction of radium substitutes of lower energy radiation, applied by after and remote loading techniques, treatment of larger volumes and of extensive and irregular dimensions can be carried out without this hazard. Not long ago the obvious difficulties in planning and dosimetry would have hopelessly overburdened our hard-pressed physicists. These can now be mastered, owing to the revolutionizing impact of the computer on radiotherapy planning. This apparatus with its capacity for rapid, repeated, and accurate calculation, has freed the physicist from his desk and allows him the use of his creative faculties. It has further provided a means of communication and of exchange of information and ideas between the "intuitive" radiotherapist and the factual physicist - the combination on which the advance of modern radiotherapy depends.

As an example, Gordon Jameson and I at the Middlesex plan to combine with Professor J. S. Mitchell and Dr. J. Haybittle at Addenbrookes Hospital, Cambridge, and with research workers at the Computer Aided Development Centre, set up by the Department of Trade and Industry at Cambridge, to develop a program for three dimensional planning of external, intracavitary, and interstitial treatment using graphic terminals linked on a time-sharing system with a large computer. We believe this arrangement to be more rational and certainly more economical than the introduction of small dedicated computers into every radiotherapy center. Gordon Jameson will be speaking later of this program, which if successful, will be of great importance not only to the large centers but also to small centers with many patients and limited staff and income. We feel that with the expected increase in number and decrease in cost of large computers, such a program could be available at a reasonable cost to all radiotherapy departments.

In the United Kingdom, a working party has been set up by the Faculty of Radiologists and the British Institute of Radiology to report on the use and advantages of radium substitutes. We have found our terms of reference to necessarily include the uses of after and remote loading.

Members of this Working Party include radiotherapists - Dr. Ian Ross, Dr. Walter Shanks, Dr. Gordon Stewart and Dr. Robert Tudway, - and physicists, Dr. Monty Cohen, Dr. Nigel Trott, and Dr. E. G. Hall of the Radiochemical Centre at Amersham. It will be appeciated that although I am often voicing my colleagues' opinions, my present paper is not an accurate account of the final views of the Committee as a whole. These will be published in due course.

While the number of cases requiring interstitial treatment have diminished greatly in recent years, gynecological intracavitary therapy still provides the large bulk of our work and is responsible for the greater part of the irradiation received by personnel in preparation and radium room, in transport through the hospital, in x-ray departments and wards. In established centers the dose received by personnel remains well below that allowed in the Code of Practice, but there is no doubt that simple substitution of radium 226 by cesium 137 sources of the same strength and dimensions is advisable in new centers. We have no reason to believe that the biological effects would differ in any way from those of radium, and dosimetry in the pelvis could be improved by the addition of shielding in the apparatus made possible by the reduced energy.

In the long run, there would be a saving of money. At the Middlesex Hospital, we have calculated that the change from hired radium 226 to equivalent cesium 137 sources bought and renewed every 15 years would reduce departmental expenses considerably after the first 8 years. The gain would be swallowed up by a recovery charge made on the return of old radium sources to the Radiochemical Centre. This charge has delayed the change from radium to cesium in British centers more than has a reluctance to change from traditional radium sources.

The introduction of cesium 137 also has the important advantage that higher specific activity allows the introduction of miniature sources. And here I must give the thanks of the whole committee to Dr. Norman Simon, who stimulated us by the demonstration of his afterloading sealed cesium 137 sources equivalent to 10 mg radium, of 15 by 1 mm dimensions, fixed to an applicator ready for afterloading.

We are also indebted to Professor Pierquin and to Dr. Chassagne for introducing us to Curietron sources and remote loading equipment, and to Professor Walstam and Dr. Cardis for introducing us to the Cervitron machine and sources. With such equipment the relationship between dose rate and radiobiological effect can be investigated, dosimetry reviewed, and irradiation of personnel completely eliminated.

While the above apparatus reproduces classic radium dose rates, a Committee set up by our Department of Health and chaired by Sir Brian Windeyer has developed the Cathetron, a remote loading device first intended for gynecological treatments and now used also for surface treatments. This machine, manufactured by TEM, was first developed clinically by Dr. D. O'Connell at Charing Cross and Fulham Hospitals in London. It was used by Professor Kunkler at Cardiff and Leeds, by Mr. Bond at Birmingham, and further developed for gynecological and surface treatment by Dr. Joslin at Cardiff, to whom I am indebted for the illustrations I am now showing.

The machine contains high powered cobalt 60 sources that deliver the traditional 24-hour dose in a few minutes. The applicators are fixed by clamps to the operating couch, and the transmission from safe to couch is mechanical. Treatment is by a few large fractions, and with adequate support for the patient and for speculum, applicators, rectal retractor, and sound treatment it soon becomes a simple procedure, carried out almost always without anaesthesia. For the patient there are obvious advantages in short weekly or twice-weekly treatments as an Outpatient, supplemented by complementary teletherapy.

At Cardiff, where there is a tradition of radium mold work, Professor Kunkler and Dr. Joslin have enlarged the use of the Cathetron to include treatment of superficial tumors earlier treated by radium molds. Here again, treatment has the advantages of convenience for patient and department, and of protection where necessary lead shielding is added to protect the patient during the passage of the source from safe to applicator.

There is now sufficient experience for us to accept the Cathetron as a safe and efficient piece of equipment, producing excellent early results in the hands of an experienced radiotherapist -- one which because of the high dose rate and fractionation provides a treatment program with advantages to busy departments and patients alike. It certainly has these advantages over remote loading equipment using slow dose rates and long treatment times. We believe that we already have sufficient clinical evidence to dispel any ethical objections to its use. But many of us are worried about radiobiological implications, and are waiting with much interest to hear the later results, both on tumors and on irradiated connective tissue and adjacent radiosensitive organs. There is no doubt that it has been introduced with great care, and that early reports -- particularly by Dr. O'Connell and Dr. Joslin and their teams -- are satisfactory.

To return to the treatments with classic dose rates, it would be a simple matter to change from radium 226 to similar cesium 137 sources, and to introduce manual afterloading. These two changes alone would reduce the hazards still present in established centers and enormously simplify the development of safety precautions in busy new centers, especially in underdeveloped countries. If even the simplest afterloading is to be used, applicators must be readily available, cheap, easily sterilized, and disposable. The effect of radiation will not matter, since each will be used once only. Dr. Burlin and his colleagues at the Central London Polytechnic adjacent to the Middlesex Hospital, are starting research with a view to developing a plastic afterloading applicator with these qualities. It will have the three different dimensions of the Manchester ovoids and of appropriate uterine tubes, be loaded through tubes reaching almost to knee level. There will be a clip fastening for the internal applicator in which the source will be permanently loaded. This internal applicator will be used many times, and must be of a material not altered materially in consistency or dimension by irradiation.

While such equipment will provide immediate improvement in protection of personnel, we look to the development of miniature sources for other improvements in technique. The introduction of miniature sources would make possible a much more flexible development of applicators. Owing to the short length of the sources, they would be curved. It would also make possible a more flexible (in another sense) use of departmental stock, which dispensed to make applicators of different lengths and, suitably interspersed with inactive sources, applicators of different linear intensities. There is, of course, a limit to variations of linear density determined by the isodose curves of the applicators. It may well be that sources of different intensities would be required in a busy department, especially if it were planned to use them for surface as well as intracavitary treatments.

In our discussions, we have considered the maximum dimensions to be limited by the need for afterloading at 3 mm - preferably less - while the minimum is governed by safety (except when permanently sealed very small spheres or cylinders provide obvious hazards) and by manufacturing difficulties (available sources sealed in steel are 2.5 to 3.5 mm in length or diameter, as those provided by the Radiochemical Centre and in the Curietron and Cervitron apparatus).

Dr. Simon's universal 10 mg radium equivalent cesium sources are narrower but more rigid, and as presently produced appear safe and unsurpassed for the Heyman packing technique, but perhaps not flexible enough for the whole departmental stock of a department.

With regard to handling hazards, we believe that miniature sources must be either fixed to an applicator (as are Dr. Simon's) or stored in a sealed container and dispensed from this into a sealed applicator, later afterloaded into the patient, or else remotely loaded into an applicator already in position in the patient. While the latter is immensely tempting, the Cathetron alone with its high dose rate and few fractionated treatments offers at present the possibility of treating all patients with one machine. The Cervitron treats only two and the Curietron only one, both with treatment durations of 1 to 3 days or so. Disconnection of the applicators when the sources are in position in the patient no doubt could be arranged, and would reduce the number of machines necessary; but this would also reduce the advantage offered by total protection of the nursing staff, and foolproof time recording.

Because of short half-life and consequent bookkeeping difficulties, we see no advantage in the routine use of iridium 192 wire sources. Cobalt 60 sources, although safer than radium, have the disadvantages of relatively short half-life and too high energy.

To sum up, opinion on intracavitary techniques among British radiologists and physicists favors the substitution of cesium 137 for radium 226, the development of miniature sources, and the introduction first of manual afterloading and later, in very busy centers, of remote afterloading. Agreement has not yet been reached on the relative advantages of high and low dose rate sources in remote loading apparatus.

Surface applicators may be increasingly replaced by external irradiation, if advantage is taken of the wide range of modern apparatus. But there remain situations - for instance, in the treatment of extensive recurrence on the curved chest wall, in the treatment of the scalp and similar areas -- where there is no satisfactory alternative treatment.

Cobalt 60 is readily available and safer to prepare. It has been used at the Christie Hospital in Manchester to provide a stock of sources to carry out surface treatment with Paterson and Parker dosimetry -- above all, so planned that on decay a suitable balance of outer and inner sources remains. There is, however, still the disadvantage of higher energy during handling and of relatively short half-life. We hope to devise a system by which a department may economically keep a balanced supply of cesium 137 sources for use on applicators with classical Manchester docimetry.

We do not see any advantage in afterloading nor in remote loading of these applicators on the patient. We would prefer to remote load the applicator with economically planned cesium 137 sources of a different intensity from those used in intracavitary treatments, and then train the patient to apply his own applicator in a room provided with suitable protection.

Iridium 192 wire is, we believe, uneconomical for application on a large scale because of difficulties in identification of used sources, and their reuse in new circumstances. But it should be available for special sites, such as applicators on the bridge of the nose where the low energy allows the insertion of light but adequate lead protection for the eyes.

Once the value of a rapid dose rate is proved, there are of course obvious practical advantages in the use of the Cathetron. But this depends on further radiobiological evidence.

Finally, I should briefly mention interstitial therapy. In the United Kingdom the use of iridium 192 as a radium substitute, the introduction of Professor Pierquin's system of afterloading, and perhaps above all the introduction of computer dosimetry, are causing a return to popularity of implants and make possible the treatment of larger and more irregular volumes and areas. We use both Manchester and Villejuif dosimetry, and enjoy the wide possibilities and (above all) the safety of these techniques.

With regard to future developments, we would welcome the introduction of afterloaded cobalt 60 or cesium 137 needles in which the sealed source is introduced into precisely inserted steel applicators. But so far we cannot foresee the introduction into interstitial therapy of direct remote loading techniques.

AFTERLOADING IN FRANCE

Daniel J. Chassagne, M.D.

In 1956, at the Gustav-Roussy Institute, we started to use the guide-gutter technique to afterload gold 198 wires in the shape of hairpins. Firstly designed to implant tonsil carcinomas, this technique soon was extended to oral carcinomas. Gold 198 wires were in use until 1960 when iridium 192 wires were designed. To date we have treated more than 1,600 cases with the guide-gutter technique, and the results are quite satisfactory. For example, there are less than 5 percent of local recurrences in mouth carcinomas (T1, T2, and small T3).

TECHNIQUES IN INTERTITIAL AFTERLOADING

GUIDE-GUTTER TECHNIQUE

This technique allows implanting either simple wire or a hairpin made of two parallel wires of iridium 192, the spacing between the two branches of the hairpin being 12 mm. The length of the guide-gutter is 3, 4, 5, or 6 cms (the most frequently used is the 4 cm length). The iridium 192 wire is 0.5 mm in diameter. The length of the active wires can be adjusted to the desired length simply by cutting the end with scissors.

Curved guide-gutter is also available for curved surfaces, such as the soft palate or palatine arch.

Mobile part of the tongue and the floor of the mouth are the main indications in tumors not exceeding 4 cm in maximum diameter therefore, T1, T2 and small T3. Guide-gutter technique is also used for carcinomas of the soft palate, uvula, jaw, and nostrils. As supplementary radiation, after a dose of 4,000 to 5,000 rads with external radiotherapy, this technique is used in carcinomas of the tonsils, faucar pillars, base of tongue, and vagina.

From 1956 to 1970 we treated more than 1,600 cases at the Gustav-Roussy Institute, two-thirds of them being oral carcinomas. At the F. Baclesse Center in Caen, beginning 1965, 276 cases were treated with this technique. At Rene-Huguenin Center in Saint-Cloud, 491 cases were treated, starting in 1962.

PLASTIC TUBE TECHNIQUE

This technique originated in New York with U.K. Henschke. It was slightly modified in 1960 for the use of continuous iridium-192 wire of 0 3 mm diameter, instead of iridium seeds in nylon ribbons. Otherwise the technique used in France is basically the same as that described by Henschke and Hilaris, with the uses of outer and inner tubes, and possibility of implantation at almost any depth, any spacing, any length, and furthermore the possibility to make loops.

Plastic tube generally is used in lesions larger than those implanted with hairpins - for instance, T3 and T4 oral carcinomas, large infiltrating lesions of the vagina, or large lesions of the skin.

This technique has specific indications, like implantation of cervical nodes or valeculla treated with the loop technique.

From 1960 to 1970, we have treated more than 1,000 cases with this technique at the Gustav-Roussy Institute. An additional 65 cases were treated with this technique at the F. Baclesse Center, beginning in 1965.

HYPODERMIC NEEDLES TECHNIQUE

This technique uses inactive stainless steel needles sharpened at both ends and introduced into the implanted volume until both ends appear symetrically outside the skin. The needles are implanted first, then the 0.3 mm diameter wire of iridium-192 is introduced into each needle. The external diameter of the needle is 0.7 mm, and this is the main advantage of this technique. Needles from 3 to 15 cm are implanted 1 cm apart. They are immobilized by means of lead shots, buttons, or plexiglass plaques.

The main indications are small skin carcinomas, carcinoma of the penis and breast. For breast cancer, interstitial therapy should be used after the usual treatment with external radiotherapy to 4 or 5,000 rads. The use of the plexiglass plaques is imperative to keep the needles parallel in soft tissues such as breast or penis.

Starting in 1967 at the Gustav-Roussy Institute, this very simple technique of afterloading has been used in over 300 cases, mostly skin cancers. The excellent results in cancer of the penis should be emphasized; we have had only two local recurrences, both in T4 tumors, in more than 30 cases treated. Thus far no local failure has been seen in the T1 and T2 breast cases treated with this technique, but there is not enough long-term followup in the breast cases for definitive results.

SILK SUTURE THREAD TECHNIQUE

Described by A.Sahatchiev in Sofia, this technique uses a simple silk suture thread holding an iridium wire 0.3 mm in diameter. The implantation is made by suturing the inactive end of each thread in the tissue. When all the threads are inserted, they are quickly pulled until the active end reaches the implanted volume. The main feature of this technique is the very small diameter (0.5 mm) and flexibility of the material.

Indications are small skin carcinomas, especially in the curved surfaces, and where the tissues are thin and fragile. The best example: implantation of the bladder.

DOSIMETRY IN INTERSTITIAL AFTERLOADING

Provisional dosimetry is always used to plan the length, spacing, and depth of the lines to be implanted. In a squamous-cell carcinoma, a dose of 7,000 rads usually is given in a volume surrounded by a reference isodose curve. This curve is determined by the percentage of the basic dose, which is the minimal dose in the center of the implanted volume (see Dr. Pierquin's paper). With the help of markers, films, and transversal seriography, calculations are made either "by hand" or by computer.

TECHNIQUES IN INTRACAVITARY AFTERLOADING

SOURCES, Two radionuclides are utilized:

(1) Iridium 192 in the 0.3 mm wire, with a linear activity of 7 to 10 mCi per cm. The flexibility of this wire allows us to afterload complex apparatus with tightly bent tubes. Accordingly, simple and straight apparatus can be easily afterloaded. The desired length is obtained by cutting with scissors a 14 cm wire. There is no contamination hazard. The only disadvantage is the relatively short half-life: 74 days.

(2) Cesium-137,shaped in a high melting-point ceramic called pollucite and hermetically sealed in a stainless steel capsule. The capsule measures 3.5 mm by 1.5 mm in diameter. The cesium grain itself measures only 1.6 mm by 0.8 mm in diameter. Source holders are preassembled with a sequence of source capsules and inactive spacer bearings to give a range of differing active lengths (see

Figure I in "The Curietron"). Each grain has an activity between 10 to 12.5 mCi, and total activity can vary between 12.5 and 150 mCi over active lenghts from 8 to 96 mm. Overall holder length is 35 cm, with a diameter of 3.2 mm; therefore this source holder can be bent very easily and afterloaded in almost any kind of applicator. These sources became available in 1969. Some centers in France already had other types of cesium-137 sources, which they continue to use.

APPLICATORS

The basic technique used at Gustav-Roussy Institute, is the plastic mold applicator that allows a special "made-to-order" applicator for every patient. Four steps are necessary to build the applicator :

(1) Molding the cavity with a liquid paste made of alginate powder and cold water which solidifies in a few minutes;

(2) Negative mold constructed with plaster;

(3) Plastic applicator with autopolymerized resin poured into the plaster; and

(4) Positioning of radioactive guides into the plastic mold applicator, and choosing the appropriate length, spacing, and depth of the sources placed in the cavity.

All the classic setups - spheres, corks, and ovoids - can be placed into this applicator. But we prefer to use nylon tubes 35 cm in length, 7 mm in external diameter, whenever possible to afterload the 35 cm cesium-137 source holder. If that is not possible,we use nylon tubes 2 to 3 mm in external diameter to afterload iridium-192.

Beginning in 1964, we have used more than 400 applicators with excellent tolerance by the patient and results that compare favorably with the old colpostat method for the gynecological indication. We also use more than 60 nasopharynx applicators, and 18 maxillary sinus applicators.

Some centers in France use other applicators, mainly the Fletcher-type applicator (R. Keiling in Strasbourg) or the modified Horwitz-applicator (G. DeLouche at the Rene-Huguenin Center, where

490 cesium-137 applications have been done since 1966).

AFTERLOADING METHODS

The simplest method would be to afterload by hand the so-called outer tube with iridium-192 or cesium-137 sources. Protection is assured by long clamps and lead screen. But protection of the nursing staff is not assured unless unloading is done every time someone enters the patient's room. This procedure obviously is not practicable for an average 6 day treatment.

We prefer to use a remote-controlled projector, the Curietron, which has been built to use the small cesium-137 source holders already described. The main features of this projector are the following :

1 - Four independent motors driving 4 cables that push 4 source holders in 4 channels,

2 - Compact and mobile apparatus to be used at bedside,

3 - Control at the entrance, to be able to put the sources back in the safe when someone has to enter the patient's room.

The time relationship of the classic Paris technique is an average of 6 days for a complete treatment. For the patient's comfort, the sleeves are disconnected from the applicator tubes during one hour per day, and the patient is permitted to get up. This is a real advantage.

Since 1969, and routinely in 1970, we have used the Curietron in 85 cases. This apparatus has achieved its purpose, since the dose received by the ward personnel has decreased to almost zero. An unexpected bonus is the change in ward morals. The radioactive patient now is considered normal by the nursing staff.

DOSIMETRY

In every intracavitary gynecological application, a computer calculation program is routinely in use for more than 2 years. It is felt that computer calculation is a compulsory method in intracavitary brachyradiotherapy. We routinely study the dose in 4 planes :

1 - The medial sagittal plane;

2 - The transferse plane passing through the cervix, visualized by seeds (L.DelClos);

3 - The oblique plane passing by the sources established according to the obliquity of the lower one-third of the uterine source;

4 - The oblique lymphatic plane is defined by G. Fletcher and R. Shalek, where a trapezoid lymphatic diagram is drawn.

The results are expressed for two areas of interest :

(a) The primary tumor area and its immediate vicinity:

1 - Dose received by seeds implanted in the cervical lips;

2 - Dose received by opacified rectum and bladder;

3 - Volume encompassed by the reference isodose 7,500 rads (1,250 rads per day, or 52 rads per hour, for a typical insertion of 6-day duration).

(b) The peripheral zones of the pelvis :

1 - Dose at the level of the lymph nodes,

2 - Dose at the pelvic wall.

After experience with more than 250 cases calculated in this manner, we feel that computer calculation is worthwhile.

USE OF AFTERLOADING TECHNIQUES IN FRANCE

Beginning in 1956 at Gustav-Roussy Institute, the guide-gutter technique and plastic tube technique have been progressively utilized in other hospitals since 1962. An iridium-192 bank was originated by the French Atomic Energy Commission in 1964, and it is really at that time that afterloading techniques came into use in many public cancer hospitals in France.

Today 11 public hospitals and one private hospital currently are using afterloading methods with iridium-192 wires. Ten other hospitals are in the process of asking permission to use radioactive artificial isotopes for interstitial or endocavitary afterloading. It should be emphasized that the laws in France regulating the use of artificial isotopes are very strict. On the other hand, for 50 years radium sources were widely used with almost no limitations -

until 2 years ago.

As for the Curietron, neither the Atomic Energy Commission which produced the cesium-137 sources nor the manufacturing company were able to sell this apparatus until a year ago. Today there are 8 users of the Curietron in France, and a few outside France.

Outside France, Gustav-Roussy afterloading techniques have been used since 1962 - 1964 in Belgium, Germany, Switzerland, the Netherlands, Italy, Spain, and England. After 1964, radiotherapists from socialist countries such as the USSR, Bulgaria, Poland, Yugoslavia, Roumania and East Germany came to the Gustav-Roussy brachyradiotherapy service under the chairmanship of Prof. B. Pierquin.

In the first trimester of 1971 the French Atomic Energy Commission is selling 60 percent of iridium-192 wires in France and 40 percent in foreign countries - including 10 american users of whom 8 are in the U. S.

The future for afterloading techniques look very bright. However, the change from the well-known radium technique to a new afterloading technique with iridium-192 or cesium-137 is not a simple one; it requires training, skill, effort and willingness - which are not always possible. It is much simpler to train young radiotherapists who will never know anything other than afterloading techniques. Of course this procedure takes more time, so widespread use of afterloading will still take many years.

ITALIAN EXPERIENCE IN AFTERLOADING

Carlo Nervi, M.D.

The techniques of afterloading were introduced into Italy in 1959, and since then have been widely employed in four centers (Pavia, Torino, Padova and Rome), in about 1,000 patients.

The purpose of this presentation is to discuss a few conclusions reached in the cases treated at the Regina Elena Institute of Rome. These results are limited to interstitial implants, as our experience with remote afterloading is too small to warrant any conclusions.

It is well known that the aim of afterloading is twofold: to improve the accuracy of the implant, and to reduce the radiation exposure to the therapist. To demonstrate whether the first goal was realized, we analyzed the percentage of local recurrences in relation to the site and size of the implanted tumor.

From 1959 to 1968, a total of 362 cases have been treated and properly evaluated. Of these, 273 patients were treated with removable implants, and in 89 cases a permanent implant was made. Iridium 192 was used in all 273 cases treated with removable implants (table 1).

Two techniques were employed: the so-called "hairpin" technique developed in France by Dr. Pierquin and Dr. Chassagne, and the "nylon ribbon" technique introduced by Dr. Henschke (table 2).

In T1 and T2 tumors of the oral cavity, even though our cases were not randomized we had the same percentage of response as with radium needles (table 3). On the other hand, local recurrence appeared more frequently in T3 lesions, especially those located in deeply seated and not easily accessible sites.

It is apparent that the results were different when the primary tumor was in the anterior or middle third of the tongue from those with tumors of the postero-lateral margin of tongue. In these cases, because of the limited space and the flexibility and collapsibility of the thin wires, it is always difficult to insert the radioactive sources into the guiding probes.

These same difficulties were also present in tumors of the pharyngeal tongue of the tonsillar fossa. In these cases, the nylon ribbon technique was not superior to the hairpin. In our opinion, radium needle implantation can be more easily carried out in pharyngeal or postero-lateral tongue lesions as the sources are more rigid. Dose distribution and local control of disease, though limited to a few patients, were better with radium needles than when employing afterloading techniques.

Afterloading was not superior in locally extensive tumors of the head and neck. Lesions larger than T3 could not be controlled better when employing afterloading techniques than could be expected with radium implants.

In superficially extensive tumors, however, afterloading is very useful. All cases of skin cancer, post-operative breast recurrence, and cancer of the vulva were treated satisfactorily with afterloading techniques. The results seemed to be better than those in similar lesions treated with radium alone.

Some neck nodes could be treated with removable implant techniques. Better results were obtained when the nodes were less than 4 cm in diameter, and not fixed to the bone.

Eighty-nine patients were treated with permanent implants (table 4). The technique employed was basically that described by Dr. Henschke: gold 198 seeds were used in 39 patients, and iridium 192 sources were inserted in 50 other cases.

Permanent implants are indicated mainly for palliation. In our experience, there has never been a cure of a primary tumor or metastatic node treated exclusively by means of implantation. Furthermore, we never had prolonged control of the disease in cases of inoperative lung or abdominal cavity tumors. However, the number of cases treated by us is limited, not so great as that of Drs. Henscke and Hilaris.

Permanent implants are most valuable when employed for palliation of neck nodes (table 5). In these cases, results are better than when employing removable techniques, since good dose distribution is reached more easily. Moreover, in palliation of extensive tumors of the oral cavity, the percentage of regression was more favorable with permanent than with removable implants.

In regard to exposure, the time spent by the therapist at a distance under 50 cm from the radioactive sources in 25 consecutive treatments was less than that spent with radium in only one-third of the cases.

We conclude from our experience that afterloading interstitial irradiation provides little improvement over conventional radium implants. Failures in deep-seated tumors are due to the difficulty of inserting the radioactive sources with adequate accuracy. In such cases radium needle implantation, even if more dangerous, is still the treatment of choice.

Occasional cures can be obtained with permanent implants but only in residual tumors. Afterloading irradiation is a real improvement only in superficially extensive tumors.

TABLE 1

AFTERLOADING INTERSTITIAL RADIATION THERAPY

SITE OF LESIONS	NO. OF PATIENTS
Lip	19
Oral Tongue	82
Pharyngeal Tongue	9
Tonsil	4
Floor of Mouth	66
Buccal Mucosa	12
Lower Gum	4
Breast (post op. recurr.)	16
Vulva	11
Vagina	9
Skin	23
Neck Nodes (N_3)	12
Abdominal Cavity	6
Total	273

TABLE 2

AFTERLOADING INTERSTITIAL RADIATION THERAPY

Removable Implants (iridium 192)

Techniques Employed

SITE OF LESION	HAIRPIN (Pierquin & Chassagne)	NYLON RIBBON (Henschke)
Lip	13	6
Oral Tongue	73	9
Pharyngeal Tongue	3	6
Tonsil	1	3
Floor of Mouth	58	8
Lower Gum	-	4
Buccal Mucosa	12	-
Neck Nodes (N_3)	4	8
Breast	3	13
Abdominal Cavity (operative exposure)	-	6
Vulva	2	9
Vagina	-	9
Skin	7	16
Total	176	97

TABLE 3

AFTERLOADING INTERSTITIAL RADIATION THERAPY

Removable Technique

SITE OF LESION	INCIDENCE OF LOCAL RECURRENCE			
	T1	T2	T3	Local stag.
Lip		0/6	3/9	3/4
Oral Tongue (Ant. 1/3)	1/9	6/25	14/30	5/5
Oral Tongue (Middle 1/3)		5/8	4/5	
Pharyngeal Tongue				9/9
Tonsil				4/4
Floor of Mouth	1/10	6/28	12/24	4/4
Buccal Mucosa	0/3	0/5	1/4	
Lower Gum				3/4
Vulva				6/11
Vagina				4/9
Skin				10/23
Breast (post op.recur.)				7/16
Neck Nodes (N_3)				5/12
Abdominal Cavity (operative exposure)				6/6

TABLE 4

AFTERLOADING INTERSTITIAL RADIATION THERAPY

Permanent Implant

SITE OF LESION	NO. OF PATIENTS
Oral Cavity	29
Lung (Operative exposure)	31
Neck Nodes	9
Abdominal Recurrences (Operative exposure)	4
Soft Tissues	16
Total	89

TABLE 5

AFTERLOADING INTERSTITIAL RADIATION THERAPY

Removable vs. Permanent Implant in Extensive Lesions

SITE OF LESION	LOCAL RECURRENCE AFTER IMPLANTS	
	Removable	Permanent
Oral Cavity (T_4)	15/18	17/29
Neck Nodes (N_3)	6/12	7/9
Abdominal Cavity	6/6	3/4

INTERSTITIAL AND INTRACAVITARY AFTERLOADING

A REVIEW OF TECHNIQUES IN SOCIALIST COUNTRIES

A. A. Sahatchiev, M.D. and M. D. Moushmov, M.D.

Information on the status of afterloading in socialist countries was collected as follows:

(1) Personal contact with radiotherapists in radiological and oncological institutes of these countries;

(2) A special questionnaire sent to the leading radiological and oncological centers and specialists, regarding the afterloading techniques used;

(3) Review of papers in radiology journals of the socialist countries.

This study included Bulgaria, Czechoslovakia, the German Democratic Republic, Hungary, Mongolia, Poland, Rumania, the USSR, and Yugoslavia. It should be mentioned that afterloading techniques are not used in Czechoslovakia, the German Democratic Republic, Hungary, and Mongolia. In this report, special stress is laid on new developments in afterloading techniques.

AFTERLOADING IN INTERSTITIAL RADIOTHERAPY

Table 1 summarizes the sources and techniques used. Afterloading in interstitial radiotherapy is used only in Bulgaria, Poland, the USSR, and Yugoslavia.

In the Oncological Institute-Ljubljana (1, 2) an interesting type of radioactive wire source is used, consisting of a nonactivated and activated part. There is a wide angle between the two parts (Figure 1A). The nonactivated portion is 5 cm long and is used as a holder. The activated parts are of different lengths: 2, 3, 4, 5, and 6 cm. The nonradioactive implant is provided in plastic tubes according to Henschke's technique (3). Afterloading is effected by the introduction of the activated part of the wire into the plastic tube so that the holder remains outside the target volume (Figure 1 B-e). Special buttons with wedges are used for fixation (Figure 1 B-f).

Pavlov, of the Moscow Oncological Institute (14), uses long plastic tubes containing at one end seeds of cobalt 60, which are introduced into the tissues with a surgical needle (Figure 2).

The afterloading techniques in interstitial radiotherapy that we use at the Oncological Research Institute in Sofia differ from standard techniques as regards the wire sources employed, the manner of their preparation, and the distribution of dose in time.

Radioactive wires with gradually increasing specific linear activity at both ends are used (15). Sources of this kind are obtained by activating them in the atomic pile through a conical cadmium screen (Figure 3). The thickness of the screen is adjusted in such a manner as to obtain cylindrical isodose surfaces coaxial to the wire. The dose distribution around these sources was established by the photoequidensic method (Figure 4a) as well as by computer calculations (6) (Figure 4b). It may be seen that the isodose curves are parallel to the source; consequently, crossing of the ends of the implant according to the rules of Paterson and Parker is not needed (Figure 5). Thus the number of the sources implanted is diminished, and radiation exposure of staff during loading is minimized. In addition, enlargement of the volume implanted in order to compensate for the uncrossed ends is avoided, and trauma is decreased.

Afterloading is accomplished with radioactive threads (7, 8, 9). An opening is made at an established place on a No. 4 or 8 silk surgical thread 80-90 cm long. A nonradioactive wire of the same length and with a diameter 0.3 mm larger than the diameter of the radioactive wire is inserted through this opening (Figure 6). This part of the thread then is dipped in a acetone solution of perchlorvinyl resin. After evaporation of the acetone and solidification of the resin, the nonradioactive wire is removed. Thus, a well-shaped and sufficiently large channel is formed into which the radioactive wire can be easily inserted. In order to completely fix the wire, this part of the surgical thread should be dipped into the resin again. The proper position of the wire into the implant is insured with a button.

The nonradioactive ends of the threads are passed through the plastic tubes and the implant is loaded, the wires being pulled into proper position by these thread ends, and their position determined by the button.

Afterloading with radioactive threads has the following advantages:

(1) The pulling procedure in loading the plastic tube implant is quicker and easier than pushing, used with inner plastic tubes (Henschke, 3) (Figures 7a, b). As the radioactive wire is inserted

in the middle part of the silk thread, readjustment is possible by pulling the appropriate end of the thread with the hands at a reasonable distance from the source (Figure 8).

(2) The radioactive part of the thread can be easily removed from and replaced in the plastic tube. If the nonradioactive part of the thread is left in the tube, irradiation may be interrupted. Removal of the implant at night thus can be avoided, since it may disturb both patient and physicians.

We have also developed a dose fractionation method in interstitial radiotherapy. In cases where there are neck metastases from primary oropharyngolaryngeal cancer (10, 11) and in primary parotid cancers, radical surgery is supplemented by intraoperative interstitial radiotherapy when there is concern that the operation may have been incomplete. Decrease in tissue tolerance because of wide dissection does not permit the application of doses exceeding 4,000-4,500 rads. If a higher dose is applied immediately after the operation, extensive necrosis is probable. That is why we delay irradiation until the surgical wound is healed. The nonradioactive implant with plastic tubes is undertaken during the course of operation. The total dose is given in daily fractions of 350-500 rads. Total doses up to 8,000 rads have been achieved without any complications.

(3) In afterloading for interstitial radiotherapy of bladder tumors (12, 13), the loading is performed while the bladder is still opened. Thus the staff is exposed to radiation during the closure of the bladder and abdominal walls. Our technique provides better protection, since afterloading with radioactive hairpins is effected after partial closure of the bladder and abdominal walls (9, 14). This technique is as follows:

The radioactive wire is inserted into the middle of a long silk surgical thread. Another surgical thread (a) is tied at the midpoint of the radioactive part of the thread. The radioactive wire then is shaped like a hairpin (Figure 9). In the nonradioactive stage of the implantation, the ends of the surgical threads which are prolongations of the hairpin are passed with a surgical needle into the bladder wall in the tumor area, and brought out through the cystostoma (Figure 10). During partial closure of the bladder and abdominal walls, the radioactive hairpin is kept in a container. At the next stage, the hairpin is introduced into the bladder wall simply by pulling the ends of the threads. These ends are tightly fixed on the abdominal wall (Figure 11A). The end of the thread which has been tied at the midpoint of the radioactive hairpin (a) is also left out of the cystostoma. The hairpin is removed (Figure 11B) by pulling the thread (a) after the other two threads have been cut off.

This technique leads to significant reduction of the dose received by the surgeon and other staff, since afterloading is postponed until the bladder and abdominal walls are partially closed. Measurements have shown that exposure at the breast level of the surgeon drops from about 40 mR, to 5-6 mR per operation. The reduction is further significant for the surgeon's hands, protected by afterloading at an increased distance.

(4) In interstitial radiotherapy of tumors of curved surfaces (nose, orbita, etc.), implantation of the radioactive thread can be performed with a common surgical needle. The radiation hazard is insignificant, and trauma to the tissues is minimal.

AFTERLOADING IN INTRACAVITARY RADIOTHERAPY

Afterloading in intracavitary radiotherapy in cases of cancer of the cervix in socialist countries is used only in Bulgaria, Poland, Rumania, and the USSR. Table 2 summarizes the sources and the techniques employed.

The hysterocolpostats used in the USSR (18-21, 23-24), Poland (16), and Bulgaria (12) are not essentially different from the standard types (Figure 12). Apparatuses for remote afterloading are being developed in the USSR (23, 24).

The technique used in the Oncological Research Institute of Sofia is a modification of the technique described by Chassagne et al (25). Instead of cesium grains or radioactive wires, we use cobalt 60 and cesium 137 (15). The individual mold is made of silicon rubber in order to achieve a higher elasticity (Figure 13). Afterloading is completed with thin plastic tubes in which the radioactive sources are inserted (Figure 14). The plastic tube is partially cut in such a way as to allow the part carrying the source to be bent at a right angle.

The conclusion may be drawn that afterloading is used in the oncological and radiotherapy departments of several socialist countries, where some new techniques have been developed.

From a radiotherapeutic point of view, our position is that interstitial and intracavitary radiotherapy of cancer needs further development; and considering radiation protection, improvement of afterloading techniques is to be encouraged.

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TABLE 1. AFTERLOADING IN INTERSTITIAL RADIOTHERAPY IN SOCIALIST COUNTRIES

Country	Sources		Techniques (References)		
	Wires	Seeds	Plastic tubes (Henschke)	Hairpins (Pierquin)	Others
Bulgaria	iridium 192 tantalum 182	-	19,21,23	24	12,18,20
Poland	iridium 192	-	4	4	-
USSR	-	cobalt 60	-	-	13
Yugoslavia	iridium 192	iridium 192	3	3	5

TABLE 2. AFTERLOADING IN INTRACAVITARY RADIOTHERAPY IN SOCIALIST COUNTRIES (Cancer of the Cervix)

Country	Sources		Techniques (References)		
	Tubes	Grains	Hystero-colpostats	Individual molds	Remote Afterloading
Bulgaria	cesium 137 cobalt 60	-	14	15	-
Poland	cobalt 60 radium 226	-	16	-	-
Rumania	radium 226	-	17	-	-
USSR	cobalt 60	-	18,19,20, 21,22	-	17,27

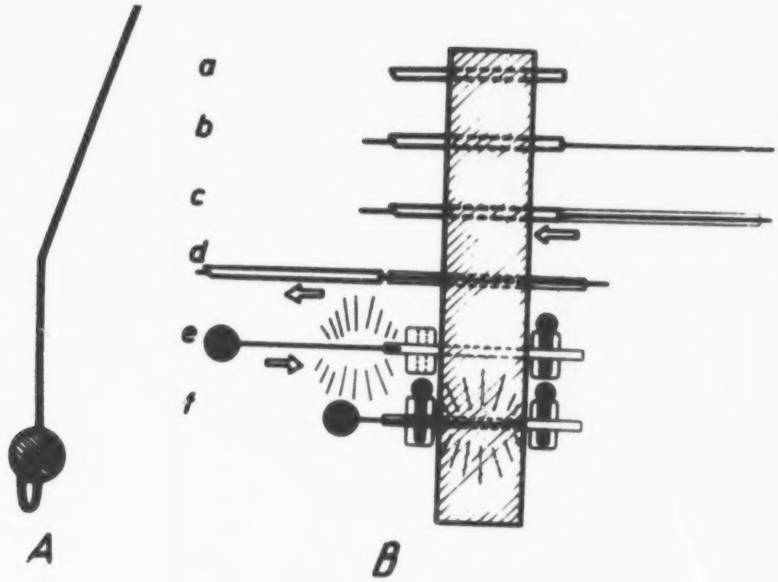

Figure 1. Technique described by Erjavec (2)
A. The radioactive wire
B. Application and fixation

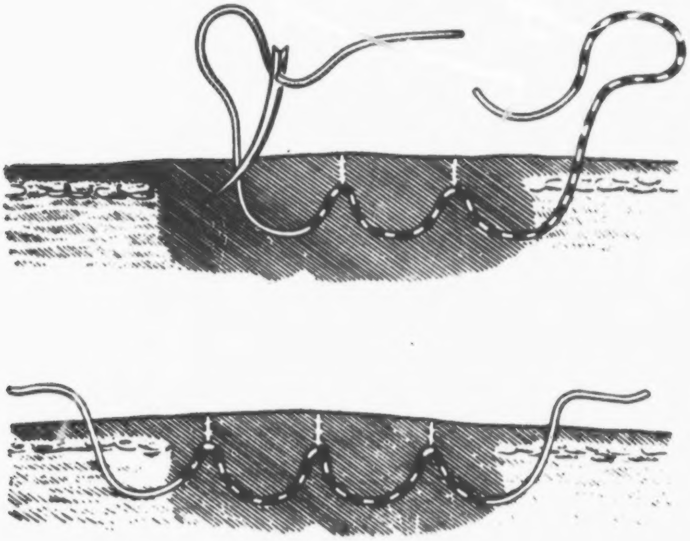

Figure 2. Technique described by Pavlov (19)

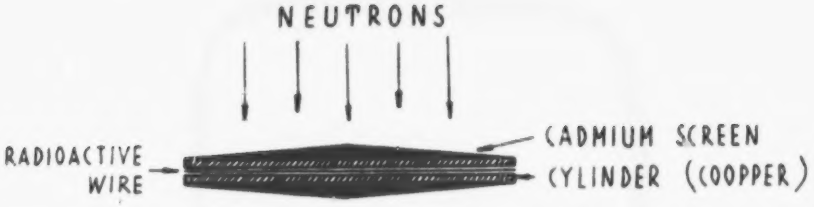
NEUTRONS
RADIOACTIVE WIRE
CADMIUM SCREEN
CYLINDER (COOPPER)

Figure 3. Cadmium screen for the production of radioactive wires with gradually increasing specific linear activity at both ends (5)

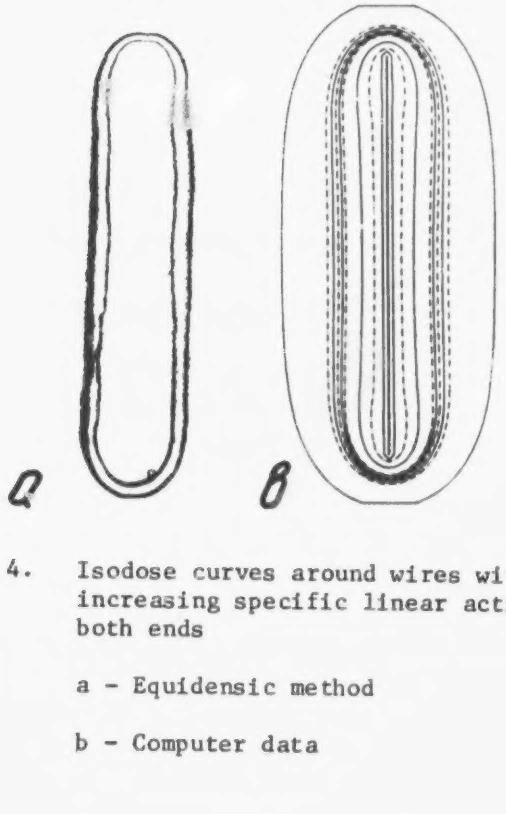

Figure 4. Isodose curves around wires with gradually increasing specific linear activity at both ends

a - Equidensic method

b - Computer data

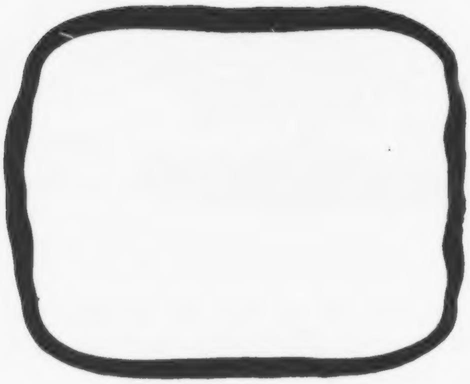

Figure 5. Equidensic curve on a plane 0.5 cm above single plane implant made by three parallel tantalum 182 wires, each 5 cm long, with gradually increasing specific linear activity at both ends

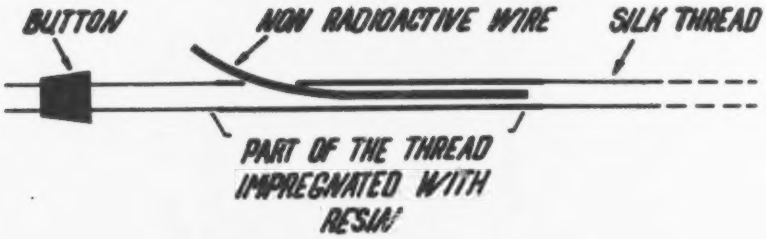
BUTTON
NON RADIOACTIVE WIRE
SILK THREAD
PART OF THE THREAD IMPREGNATED WITH RESIN

Figure 6. Preparation of a "radioactive thread"

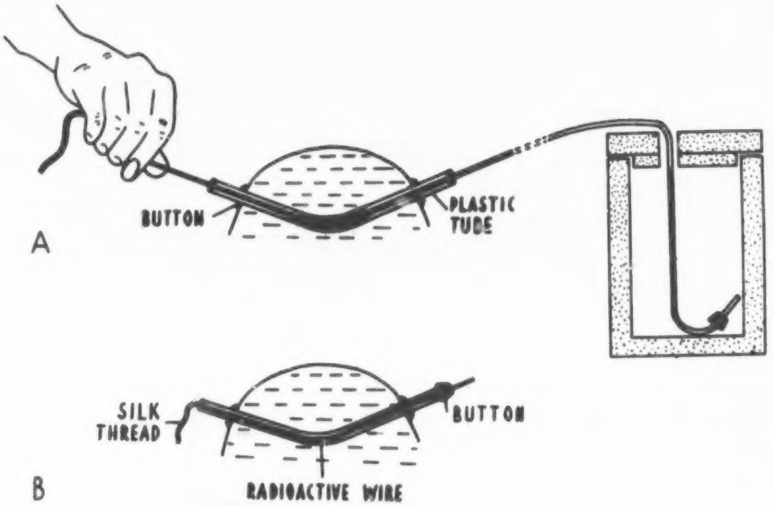
BUTTON
PLASTIC TUBE
A
SILK THREAD
BUTTON
RADIOACTIVE WIRE
B

Figure 7. The radioactive part of the thread is loaded into the plastic tube by pulling the surgical thread instead of pushing.

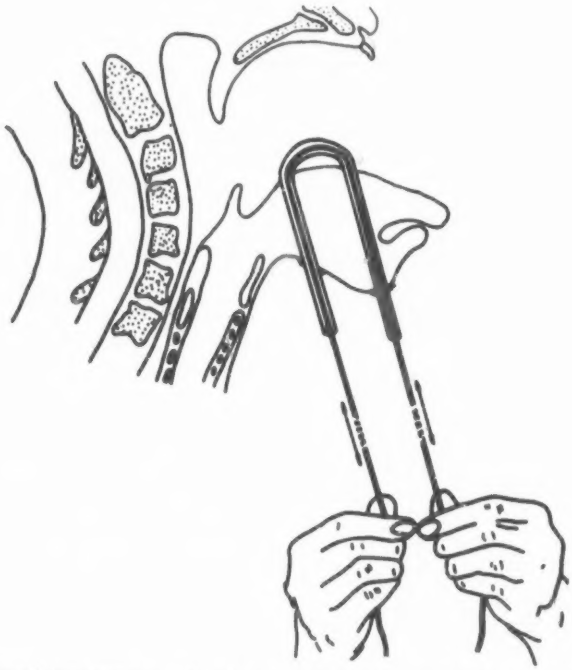

Figure 8. Readjustment of the radioactive part of the thread

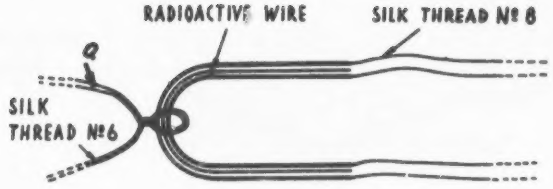
RADIOACTIVE WIRE
SILK THREAD Nº 8
a
SILK THREAD Nº6

Figure 9. Hairpin for implantation into the bladder

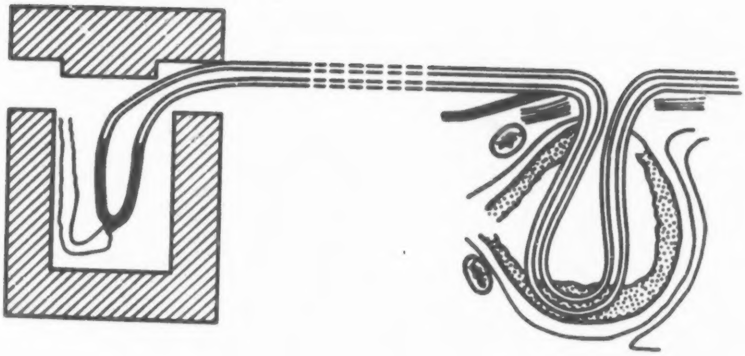

Figure 10. Nonradioactive stage of implantation of the radioactive hairpin into the bladder

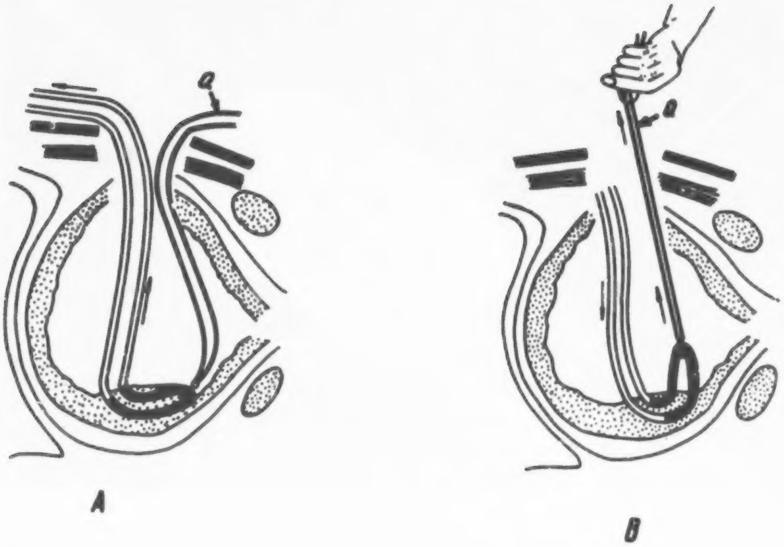

Figure 11. A - Fixation of the radioactive hairpin
B - Removal of the radioactive hairpin

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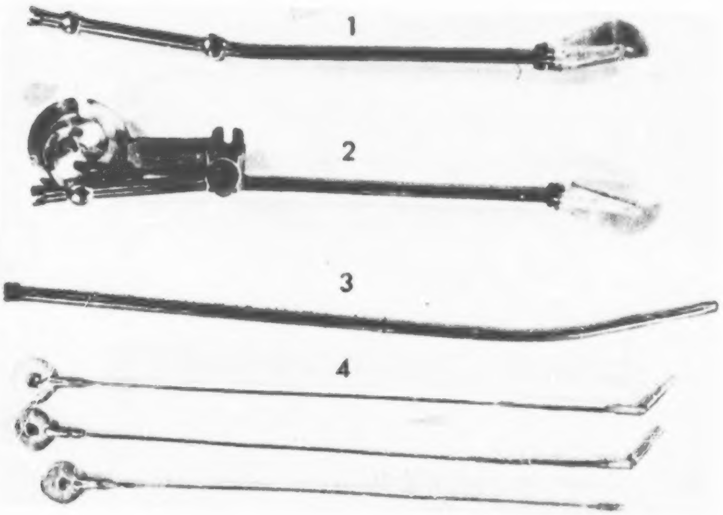

Figure 12. Hysterocolpostat with afterloading described by Mitrov et al. (14)

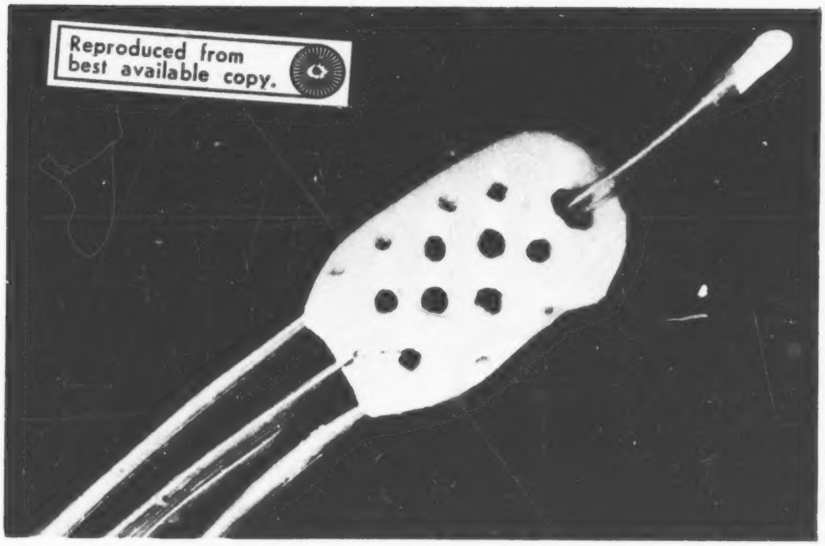
Reproduced from best available copy.

Figure 13. Silicon rubber individual mold (15)

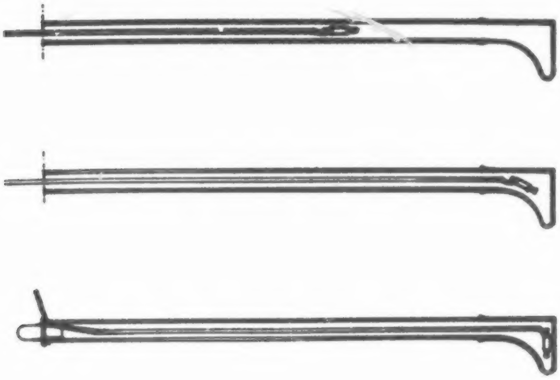

Figure 14. Loading the radioactive tubes into the individual mold

THE STATUS OF AFTERLOADING IN LATIN AMERICA

José Noriega-Limón, M.D., D.M.R.

In order to get some idea on the status of afterloading techniques in Latin America, a questionnaire was sent to 19 centers in that area. The following information was requested:

1. Was afterloading used?
2. If in use, what type of technique was practiced?
   (a) Simple removable or permanent manual
   (b) Remote controlled, either with complete or incomplete protection
3. Was it used for the treatment of carcinoma of the cervix? What technique and what radioactive material was used?
4. Was afterloading used for interstitial implants?
5. What were the advantages observed?
6. What were the problems?
7. Could afterloading techniques be considered useful for Latin American countries?
8. If afterloading was not used, why not?
   (a) Lack of equipment
   (b) Lack of information
   (c) Considered of no value
   (d) Complication of established routines
9. Was information or technical help desirable?

Only 11 departments of Radiotherapy replied. Their answers are summarized in Tables I and II.

TABLE I

AFTERLOADING
Status in Latin America

In use	3
No use	8
Simple manual	3
Remote control	0
In ca. cervix	3
Implants	2

TABLE II

AFTERLOADING
Status in Latin America
11 Centers

Considered useful	9
Doubtful value	2
Lack of equipment	7
Desire for technical help	8

It can be seen that only 3 centers were using afterloading at the time of the inquiry, and all three are in the same country. This is quite surprising, considering that the incidence of carcinoma of the cervix in some Latin American countries is the highest in the world, and afterloading techniques are desirable in the treatment of this malignancy. The number of cases of carcinoma of the cervix reported varied from 100 to 650, the average being 402 per year per center in this part of the world. A simple manual removable afterloading technique was reported by the three centers. None of them was considering purchase of a remote control apparatus. The procedure originally was used in four centers but one of them has discontinued it, considering their present technique was unsatisfactory and planning to resume it in the near future, after improvement of their applicator.

None of the centers are using commercially available afterloading applicators, such as those of Drs. Henschke or Fletcher, on the grounds that they are not easily obtainable or that they are rather expensive. Home-made afterloading devices were in use in the centers practicing the method. Two centers have developed an intrauterine applicator associated with plastic colpostats. It is simple polyethelene tube with a diameter large enough to permit the introduction of another polyethelene tube containing the radioactive sources or dummies. The external tube is introduced in the uterine cavity at the operating theater, with dummies in the inner plastic tube. After films are taken and the patient is returned to the ward, the dummies are withdrawn and another tube containing radium sources is inserted in their place.

The vaginal applicators are separate ovoids of a plastic material in three sizes: small, medium and large (as in the Fletcher techniques). They have a long plastic tube that acts as an arm to manipulate them, and for the introduction of a thinner tube containing dummies or radioactive material. The inner tube has, at one end, a dummy or radium source. When pushed along in the outer tube and introduced into the colpostat, it bends along the main vertical axis of the colpostats. The principle is the same as in the Fletcher afterloading system, but no metal or mechanical device is used.

Another center has developed an applicator similar to that designed by Bloomfield in England some years ago. It is a sort of phallic applicator that fills the vagina to the vault, ending in two rounded ends. It has a central orifice along the main axis through which a central tube passes to the uterine cavity and to the lateral one, permitting access to the rounded lateral upper end and acting as colpostats. The vaginal sources are placed parallel to the intrauterine tandem, rather than the standard position. The rectum is protected by a tungsten or a lead shield built into the applicator.

Existing radium sources have been used in the two types of applicator described. A new center in Mexico City is planning to use the Fletcher applicator with cesium sources.

From opinions expressed in the inquiry regarding carcinoma of the cervix, the general feeling is that afterloading has a place in centers where the patient load is high. On the other hand, 6 centers reported that staff exposure has been well below the permissible dose, in spite of the large number of patients treated by traditional methods, without afterloading. Nine centers considered afterloading desirable but not indispensable in the treatment of carcinoma of the cervix.

Our personal opinion is that the reduction of exposure to the staff and in the operating room, permitting more careful application and better control of the position of the sources during treatment, is more than enough to recommend the use of afterloading by simple manual technique in the treatment of carcinoma of the cervix.

The use of remote control afterloading apparatus is attractive, particularly those that give complete protection in the ward. Their high cost and lack of local maintenance service make them inadvisable for Latin American countries at this time. Regarding afterloading of high specific activity radionuclides with high doses at short times, it was the general (and my personal) feeling that it would be premature to recommend them for use in Latin America until the results were statistically better and showed less morbidity than those obtained by modern, already established, methods of radiation. The criteria for use of this new modality should be based on these two parameters, more than on purely physical, mechanical, or economical ones, or the simple novelty of the procedure.

In regard to interstitial implants using afterloading, only two centers in Mexico used it. One followed Dr. Henschke's method, and the other (our own Department) followed Dr. Pierquin's system, using hairpins and wires of iridium 192, according to the location of the lesion. In our experience, this has been of particular value in carcinoma of the oral cavity, cheek, floor of the mouth, and tongue, as well as to implant residual masses after external irradiation. It has proven useful in the treatment of carcinoma of the female urethra, and metastasis in the lower vagina. The morbidity is nil, patient tolerance is high. Implantation under local anesthetic makes the procedure extremely simple, in most cases. Use of the "snail" type curves permits complete distribution around the source, in centers with no access to a computer.

In one plane implant, the use of the Paterson and Parker method permits fairly good dosimetry, if low filtration is allowed for, and the distribution curves published by Pierquin are taken into consideration around the ends of the pins and upper part of the hairpins, where a hot spot is formed.

Afterloading has not been used due to lack of equipment in 8 centers, and lack of information in 3. All departments express the opinion that the method should be more widely used in this part of the world. They wish to have more information, and when possible, technical advice by visiting radiotherapists and practical demonstration, or facilities for short training abroad.

To sum up, afterloading techniques are not widely used in Latin American countries. More common use is desirable, particularly in the treatment of carcinoma of the cervix, a predominant malignant neoplasm in this area. Simple manual afterloading techniques are highly recommended for Latin American countries. Remote control methods, particularly those using large quantities of radioisotopes of high specific activity, are for the time being not indispensable, and should prove their value by showing higher survival rates and less morbidity than traditional methods before they can be recommended for use in this part of the world.

DISCUSSION

DR. H. L. KOTTMEIER: I would like to thank you for inviting me to this important meeting, and to make a few comments on the use of afterloading. I think that it's very important that scientists are beginning to realize its significance, and that we are able to discuss this very important problem, which has so many different aspects.

My remarks will be limited to gynecology, since we have no experience with the implantation of needles or other material in tumors of any other kind. Implantation techniques were very much used in the Radiumhemmet in earlier years, but not in the recent 25 years.

The problems involved, as Dr. Simon pointed out in the beginning, are considerable. One is protection. Another, which Dr. Snelling mentioned in her excellent presentation, is variation in the intensity and fractionation involving important radiobiological problems that we know very little about at the present time.

If we are going to use afterloading -- and I think we should -- I would like to bring up some questions. I'm not going to discuss in detail its use in gynecology. I will leave that for tomorrow, when I will present the subject of afterloading of carcinoma of the cervix, as well as carcinoma of the corpus. Now I would like to make some general remarks.

We have many methods to protect the operator and the nurse, but the problem remains for ward personnel. We haven't been able to decrease the dose to the ward people in manual afterloading in spite of everything we do -- at least in such large institutions as the Radiumhemmet, where we treat about 15 patients a day. The problem is in the ward, there is no problem as far as radiation exposure in the operating theater is concerned. Therefore, we believe that manual afterloading has limited value in the treatment of carcinoma of the female pelvis.

As Dr. Simon pointed out in his magnificent paper, the problem is how to control the radium or cesium or whatever you use (we use cesium) so that it is in correct position. Various techniques have been developed. We have used afterloading for 12 years, and in spite of the very careful control of dose distribution, and x-ray films, we have been inaccurate at times. We were convinced that we had inserted cesium in the correct position in one patient; everything was to favor this. But it was not, and she sustained severe damage to the lower vagina and skin of the thighs.

The third point I would like to bring up for discussion here is how to fix the radioactive material in the patient with routine treatment of afterloading. In the technique developed at Gustav-Roussy, the vaginal mold is made prior to treatment. This makes it possible for the patient to move, which is a great advantage. The French have developed the use of this mold, which we have tried in selected cases with the close collaboration of Gustav-Roussy. The mold will help us avoid the urethral complications we have had from the earliest days.

A fourth point I'd like to stress is that when we treat carcinoma of the cervix by remote afterloading, the uterus is in a different position from what it is in patients to whom we apply routine radiation therapy.

I mention these four points because in our experience they are extremely important. We have used remote afterloading for 11 years, and we have seen more complications in these cases than in any other cases. To some extent, it may be that we have increased radiation intensity. But many problems remain.

I am very much in favor of remote afterloading. I think it will be the method of choice in the future. Many problems remain, and they are not so easy as you might think.

CHAIRMAN SIMON: One of the earliest experiences in making molds and tailoring a mold to the vaginal anatomy was here in the U. S., perhaps a quarter of a century ago, by Dr. Twombly. You may want to reserve your discussion for the session on carcinoma of the cervix; however, would you care to comment on molds in the anatomy in the pelvis, Dr. Twombly?

DR. TWOMBLY: I'd like to ask Dr. Chassagne if he would tell us a little bit more about what he does after he gets the mold. We have made a very elaborate lucite mold that is quite complicated and costs about $35 to produce. I would like to know how he has solved this problem.

DR. CHASSAGNE: I think you should see the film that Dr. Pierquin brought. I would point out that the cost is only $6-8. In our routine, we do not need special things. Plaster of paris is available everywhere. Something to put inside the plaster: either rubber silicone, as Dr. Sahatchiev does, or our resin which is autopolymerized, is satisfactory. It hardens in approximately 10 minutes, and the whole process is completed in 30 minutes. So I don't think it costs too much. We routinely make two or three molds per day.

DR. PIERQUIN: Yes, I have a comment for Prof. Kottmeier, since he spoke about the problem of manual removable afterloading. I think that the manual method is suitable for iridium, where you have only 0.3 Mev gamma energy. It is possible to transport sources of iridium without any irradiation of the nurse or medical personnel.

I have had experience in my new department with techniques of vaginal molds iridium, and with removable afterloading. My nurse gets little measurable radiation with this technique, because the low energy of iridium allows protective shielding in a lead box about 4 cm in thickness. The sources can be removed once or twice a day and put inside the box in perhaps one or two seconds for each wire. With the added protection of a mobile shield of lead, there is little exposure.

I think the fundamental factor in any utilization of active sources is real protection with a mobile shield of lead.

DR. HENSCHKE: I want to express my gratitude to our friends for presenting such an interesting picture of afterloading in Europe. Afterloading originated in the U. S., but it really has bloomed in Paris and spread from there. So we have to pay our special respects to Dr. Pierquin and Dr. Chassagne.

I think we would all agree that the most important application of afterloading is in intracavitary use, and especially in carcinoma of the cervix. One important question in carcinoma of the cervix is whether remote afterloading or manual afterloading should be recommended for general application. Dr. Kottmeier, with whom I usually agree, seems to think that remote afterloading is the thing to do. Dr. Noriega strongly made the point that remote afterloading is not suitable for the developing countries.

When we talk of carcinoma of the cervix, we should keep in mind that this essentially is a disease of the poor. You see it in the U. S. twice as frequently in blacks as in whites; in South America and China, carcinoma of the cervix constitutes about 30 percent of all cancers treated in radiotherapeutic institutions.

I think remote afterloading is completely out of question in developing nations. Dr. Snelling made the point very well, and we should take essentially the same attitude. Remote loading is a very tricky procedure, you have to take extreme precaution to see that the source is in the right spot. It is biologically uncertain, there have been quite a few bad experiences at Memorial Hospital with high dose rates. You have to go to many fractionations, which we do not like to do in developing countries, where we like to get everything over in one application.

So I think remote afterloading at this stage should be a research project strictly reserved to a few big institutions. You can make simple afterloading so quick and certain that the exposure is negligible. With our applicator, we get less than one mrem putting the source in. In fact, we can't even measure it.

I don't want to disagree with Dr. Pierquin, but I don't think there really is much difference between cesium and radium as far as protection is concerned. I think it is important to change from radium to cesium. Cesium sources fit a model applicator and simple afterloading devices. You can put the cesium sources in and out once a day by hand, and stay under permissible exposure levels.

Interstitial implantation is completely different. It is a very difficult procedure, and I think we owe special thanks to Dr. Nervi for bringing out that afterloading in interstitial therapy does not necessarily yield better results or less exposure. In fact, you can get poor results and a lot of exposure. Maybe you don't get exposed as a physician, but personnel who load the sources might get it. So I think we have to realize that afterloading in interstitial therapy is a highly complex and difficult procedure. If you are not really set up for it, you are much better off with needles. I think the very excellent results obtained in Paris are only because brachytherapy has become a specialty.

At Howard University, we have set up a division of brachytherapy and teletherapy. It requires a special person, special interest, special skills, special personnel -- you just can't do it in haphazard fashion. I'm sure that other places have bad results with afterloading. In cervix cases, the position in many applicators is very uncertain.

I think it is very good that we speak up at this conference to find and point out the dangers of afterloading.

DR. TWOMBLY: A number of years ago at Memorial Hospital, with Dr. Quimby's help, we compared the effects of interstitial needles with high and low dose rates in the treatment of cancer of the cervix. With high dose rates we got necrosis of the bladder, rectum, and cervix -- many complications, and the cure rate was poor. Shortly afterward I went up to Presbyterian Hospital in New York and took part with Dr. Corscarden in the implantation of needles into the parametria, and didn't see these complications. To my mind, this meant that I was observing the difference between high and low intensity irradiation.

The interstitial needles used in treatment of the parametria at Presbyterian were of such low intensity that they were left in place for 6 to 7 days. The needles used at Memorial were of such high intensity that they usually were left in place less than 24 hours. I would say, therefore, that the use of afterloading techniques with very intense sources such as those proposed by Dr. Windeyer may be very, very dangerous.

COMPUTER APPLICATIONS

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COMPUTERS IN RADIOTHERAPY

Arvin S. Glicksman, M.B., M.D., D.M.R.T.

It has been demonstrated in industry as well as science that many simple repetitive tasks and some more complex nonrepetitive tasks can be performed more rapidly, accurately, and precisely when they are assisted by automated or semiautomated systems. Within the framework of present day technology, these concepts may be adapted to the care of patients with cancer by the cooperative effort of the radiotherapist, the radiological physicist, the electronics engineer, and those concerned with computer sciences. Not only can the many components of the total process of radiotherapy be automated, but it is now reasonable to project a completely automated system which would allow for the rapid selection and execution of optimal treatment technique for each patient, based upon the first-hand knowledge and insight of the clinical radiotherapist.

In providing optimal treatment, i.e., designing strategies for the use of ionizing radiation which will lead to the most desirable results in the treatment of cancer, external beam therapy has been hindered by a number of obstacles: uncertainty as to the volume to be irradiated, attaining a dose distribution throughout the target volume most suited for the particular tumor, difficulty in manipulating with ease and precision the patient-machine complex for diverse and changing interrelationships. These difficulties, for the most part, are not applicable to situations where interstitial or intracavitary radionuclides can be applied. There are inherent problems in terms of the handling of the radionuclides, such as unwanted and unwarranted exposure to medical and paramedical personnel. To a large degree, this can be controlled by the afterloading techniques discussed at this conference.

It is most fortuitous to bring together one of the oldest and most successful forms of treatment and the newest computer assistance, with the prospect of enhanced effectiveness of both. Three years after the discovery of radium, Pierre Curie immediately saw the medical implication of the famous Bechquerel skin reaction and gave a supply of radium to Danlos at the Hospital St. Luis in Paris. It was Alexander Graham Bell who first suggested in 1903 that radium be placed in sealed capsules that could then be inserted into tumors. Since then a whole system of treatment has developed.

The first application of computer technology to the calculation of dose distribution for radionuclides was in the Physics Department of Memorial Hospital, in the late 1950s. K.C. Tsien had demonstrated the feasibility of external beam isodose computation, and members of Dr. Laughlin's group--particularly May Lou Meurk and Richard Nelson--developed computational methods for interstitial and intracavitary radiation.

It is particularly appropriate that the first real program for interstitial seeds involved afterloading technique. William Siler relates that at 3 o'clock one afternoon Dr. Henschke asked for a dosimetric calculation for a patient in whom he had put nonradioactive ribbons, so that proposed irradiation could be discussed the next morning. Using a Bendix Corporation computer and working all night, Mr. Siler was able to give Dr. Henschke three planes of the implant by 8 o'clock the next morning.

In the next decade many advances of computer applications to isodose computation occurred, both for the external beam and interstitial and intracavitary treatments.

If afterloading techniques have an advantage in reducing exposure to personnel, the application of computer technology to afterloading techniques has potential for optimizing treatment of the patient. By rapidly making available a three-dimensional dose calculation, the computer allows the radiotherapist to alter the physical arrangement of the radioactive materials, or alternatively to alter the time of application of each of multiple sources. Hot spots and cold spots thus can be known in advance, and modified before the patient is exposed to ionizing radiation. This obviously would be quite difficult if the radiotherapist had to manipulate radioactive sources rather than dummy sources during the optimization procedure.

The computer can be used not only as a substitute for the dosimetrist, but also as a library of previous techniques that can be perused to find radionuclide applications that have met with the best success. The radiotherapist can ask the computer to compare the present setup with prior ones, he can alter current application to yield the most successful results. This reinforcement of the radiotherapist's memory extends his resourcefulness for each patient.

The opportunity to integrate and improve the many decisions necessary in radiotherapy is a major consideration. The most magnificent accomplishment of computer technology is that it promises to return and enforce control over his decisions to the physician. He is given the ability to define, control, and constantly monitor management of the patient for whom he is responsible. It is generally agreed that computer technology offers the radiotherapist considerably broader horizons, whether with dedicated small computers or on-line to large computer facilities, for total systems or for the many small parts that make up the whole of radiotherapy.

The basic question is not what can be done, but rather what needs to be done. We have the opportunity to use the computer both as our slave and our savant, and thereby to enhance the effectiveness of radiotherapeutic techniques in the cure and control of cancer.

USE OF A COMPUTER FOR DOSIMETRY IN INTERSTITIAL AND INTRACAVITARY RADIOTHERAPY

Marilyn Stovall, B.S. and Robert J. Shalek, Ph.D.

The widespread use of electronic computers has made possible a new approach to the assessment of radiation dosage from interstitial and intracavitary sources. For the first time complete dose distribution comparable to those available for external beam treatments are calculated for individual patients. The introduction of computers has resulted in a new look at the parameters used in the calculations, with some changes based on more recent physical data.

The purpose of this paper is to review briefly the status of computer programs in general, with specific comments on the computer technique used at the University of Texas M. D. Anderson Hospital.

I. HISTORY AND BACKGROUND

Because of the short treating distance, the special problem of dosimetry in interstitial and intracavitary therapy is that the geometry of the sources is critical. Each implant is unique, and requires an individual calculation based on the geometry of the actual implant. The dose distribution is complex, and calculation of dose to more than a few points by hand is too time-consuming and tedious to be a routine method.

To cope with the problem of brachytherapy dosimetry, two manual systems of calculation were developed beginning in the early 1930s: the Quimby system (1-3) and the Paterson-Parker system, which has been more widely used (4-3). In either of these systems, if one implants sources according to particular rules, the dose rate to one point may be easily calculated using special tables. Because the point of dose specifications is meaningfully related to the implanted sources, radiotherapists have been able to correlate clinical results with the single dose calculated, and the manual systems have had widespread clinical success.

With the availability of electronic computers, it became practical to calculate the complete dose distributions around arrays of sources for individual patients. The first paper reporting such work was published in 1958 by Nelson and Meurk (9). Numerous papers have appeared since concerning various computer techniques; most of these are listed in Table 1, with a summary of their salient features.

The computer method used at the University of Texas M. D. Anderson Hospital has evolved over several years (10-14). Radiographs of three typical implants are shown in figures 1-3. The output data shown for each was computed using this program (RADCOMP).

II. PRESENT STATUS OF COMPUTER PROGRAMS

As shown in Table 1, the various computer methods for brachytherapy dosimetry are remarkably similar. Although this is not an exhaustive list, and the authors do not claim that it is complete, the data show that the differences can be summarized under three headings: methods of deriving input data, method of calculation, and type of display of output data.

A. Method of Deriving Input Data:

The use of radiography to localize sources after implantation has been the standard method both with manual systems and computer calculations. The radiographs may be orthogonal views (7, 15, 16), stereographic views (17, 18), or transverse tomograms (19-21). The computer methods reported in the literature use one of these sets of radiographs to derive input data, and at least two programs allow the option of using more than one type of radiography. Orthogonal radiography was used for the examples in figures 1 and 2, stereoradiography was used in figure 3.

The increased precision obtained by computer methods has emphasized the need for careful radiography (14, 22-24). A sophisticated computer program does not assume that the geometry of radiography is correct; if the computer cannot be programed to correct an error, there should be an error message that indicates the need for repeat radiography. One program automatically identifies and localizes sources using orthogonal radiographs (25).

B. Method of Calculation:

The gamma radiation reaching a given point from various portions of a filtered line source vary inversely as the square of the distance from each portion of the source, and will be reduced exponentially according to the thickness of filtering material in the path of the radiation. The source may be divided into an infinite number of sections, and then integrated over the length. This results in an integral solved numerically by Sievert (26) and has appeared in tabular form in other publications as well (13, 27-30). This is the classical method of calculation, and is the basis of the Paterson-Parker tables and other data (13, 30, 31).

As an alternative, the calculations may be simplified by dividing each source into a small number of segments, usually 2 to 4, with each segment considered as a point source. At distances more than twice the length of the point source segment, this method is sufficiently accurate. Therefore, it is acceptable for gynecological intracavitary sources where the region of interest usually is greater than 2 cm from the sources. However, this method is not adequate for interstitial needle implants where the region of interest is usually at 0.5 cm distance. Of course, if one divides a linear source into a large number of point sources, the results will be identical to those obtained with the Sievert integral. Radioactive seeds are considered as single point sources in all programs handling this type of calculation.

Because of the similarity between most programs, one would expect calculations to be in good agreement. However, only one publication has attempted such an evaluation; Powers et al (33) compared four widely used computer methods (34-37) and found the programs were in good agreement and had adequate accuracy for clinical purposes.

C. Type of Display of Output Data:

The form of output data varies with different programs, depending upon the hardware available. In general, the problem is to present to the radiotherapist a display of the dose distribution in one or more planes about the sources. Data presented in the form of isodose curves are most easily assimilated, and they can be drawn automatically by a plotter. The program also plots the locations of sources, and anatomical landmarks for orientation. The output data shown in figures 1-3 were drawn automatically by an incremental plotter.

Although automatic plotters are becoming less expensive, the cost is still prohibitive for many institutions. Output may be limited to a line printer. In this case, dose distribution may be displayed by printing the same character at points of equal dosage or by listing the dose rates at various coordinate locations, allowing the user to draw isodose curves manually. In addition to these methods of producing hard-copy output, at least one system uses a cathode-ray tube to give an immediate display of dose distributions, an advantage if one needs data quickly (38).

III. USE OF COMPUTER-GENERATED DATA AND RELATIONSHIP TO MANUAL SYSTEMS

In a sense computer calculations represent a new system which may be independent of the manual systems. However, in order to preserve the 40 years of clinical experience with the older methods, it is important to understand their relationship to complete distributions calculated by computer. As an example, we will consider here the correlation between the Paterson-Parker system and computer generated dose distributions produced by RADCOMP (12-14). There are two principal considerations: the quantitative difference, and the spatial relationship.

A. Quantitative Difference:

The Paterson-Parker system was derived to express dosage in roentgens in air, did not allow for the absorption and scattering of radiation in tissue. In addition, certain approximations were used in constructing the tables. Following the recommendations of the ICRU (39), the computer program calculates dosage in absorbed dose (rads) in muscle. To compare the results of the two methods quantitatively, four factors must be considered:

(1) Specific Gamma-Ray Emission:

The Paterson-Parker tables were prepared using 8.4 roentgens per hour as the dose rate in air from a point source of radium filtered by 0.5 mm platinum. More recent measurements indicate that this dose rate is 8.25 roentgens per hour, which is the value used in the computer program. Thus, the dose rates derived from Paterson-Parker tables should be reduced by the ratio of 8.25/8.40.

(2) Oblique Filtration:

In the preparation of the Paterson-Parker tables, the attenuation of dose due to oblique filtration was not completely allowed for (40, 41). The dose calculated by the computer is approximately 2 to 4 percent less than calculated by the Paterson-Parker tables.

(3) Attenuation of Gamma Rays in Tissue:

Since the Paterson-Parker tables give exposure dose in air, no allowance was made for the attenuation of gamma rays in tissue, which is about 1 percent centimeter for gamma rays of radium up to a distance of 4 cm (42).

(4) Absorbed Dose:

For radium, the exposure dose in roentgens is multiplied by 0.957 to obtain the absorbed dose in muscle expressed in rads (39).

When all of the above factors are considered, the multiplicative correction factor to convert Paterson-Parker dose in roentgens to rads in muscle is 0.90 for interstitial implants with treating distances less than 2.5 cm. For cervical applications, where the region of interest is usually greater than 2.5 cm, an average factor to convert Paterson-Parker roentgens to computer rads is 0.93.

Using a different method of analysis, Porter (43) suggests using 0.92 as the rads per Paterson-Parker roentgen. This is essentially in agreement with the above figures.

B. Spatial Relationship:

During the transition from the Paterson-Parker system, with a single "stated" dose rate, to computer calculations giving the complete distribution, it is important to understand the location of the point of dose specification for planar and volume implants in the Paterson-Parker system. The stated dose for planar implants is 10 percent above the minimum dose in the plane of calculation. The stated dose for volume implants is 10 percent above the minimum dose in the implanted volume. If one multiplies the Paterson-Parker stated dose rate by 0.90, as discussed above, the isodose curve in the complete distribution which has the value of the stated dose is consistent with the Paterson-Parker rules. The important point is that before using complete distributions clinically, the therapist must understand the location of the point of dose specification used previously. When first presented with complete distributions, the radiotherapist may be tempted to select a total treatment dose that will include all of the area in the plane of calculation, or all of the implanted volume. This would result in overdosage of at least 10 percent if he is basing his prescription on clinical results obtained with the Paterson-Parker system.

Of course, the Paterson-Parker tables are valid only for implants that follow the rules of the system in regard to geometry and distribution. The main value of computer calculations is for implants that do not follow the rules, either by design or error. In a retrospective study of approximately 100 oral cavity implants, almost 80 percent of the complications, either recurrences or necrosis, could be explained on the basis of dosimetry (44). All of these implants deviated from the Paterson-Parker rules to some extent, but that system was used for dose control. Since 1960, individual dose distributions have been calculated by computer for all patients receiving interstitial or intracavitary therapy at the University of Texas M. D. Anderson Hospital (45-47).

In general, when changing from one dosage system to another, either manual or computer, it is imperative that the user analyze the differences between the systems before he attempts to transfer clinical experience. For this reason, the introduction of computer dosimetry can be a traumatic experience during the transition period, before the radiotherapist becomes accustomed to seeing the complete distribution.

IV. FUTURE DEVELOPMENTS

It is not likely that there will be major changes in the method of calculating dosage around interstitial and intracavitary implants. The current need is for faster turnaround time for computer calculations through the use of automatic data recording, time-share computing, and instantaneous display of output data. Rapid availability of dose distributions with the use of afterloading applicators would allow the therapist to vary the loading and time to optimize treatment, and would be particularly useful for afterloading with high-activity sources and short treatment times.

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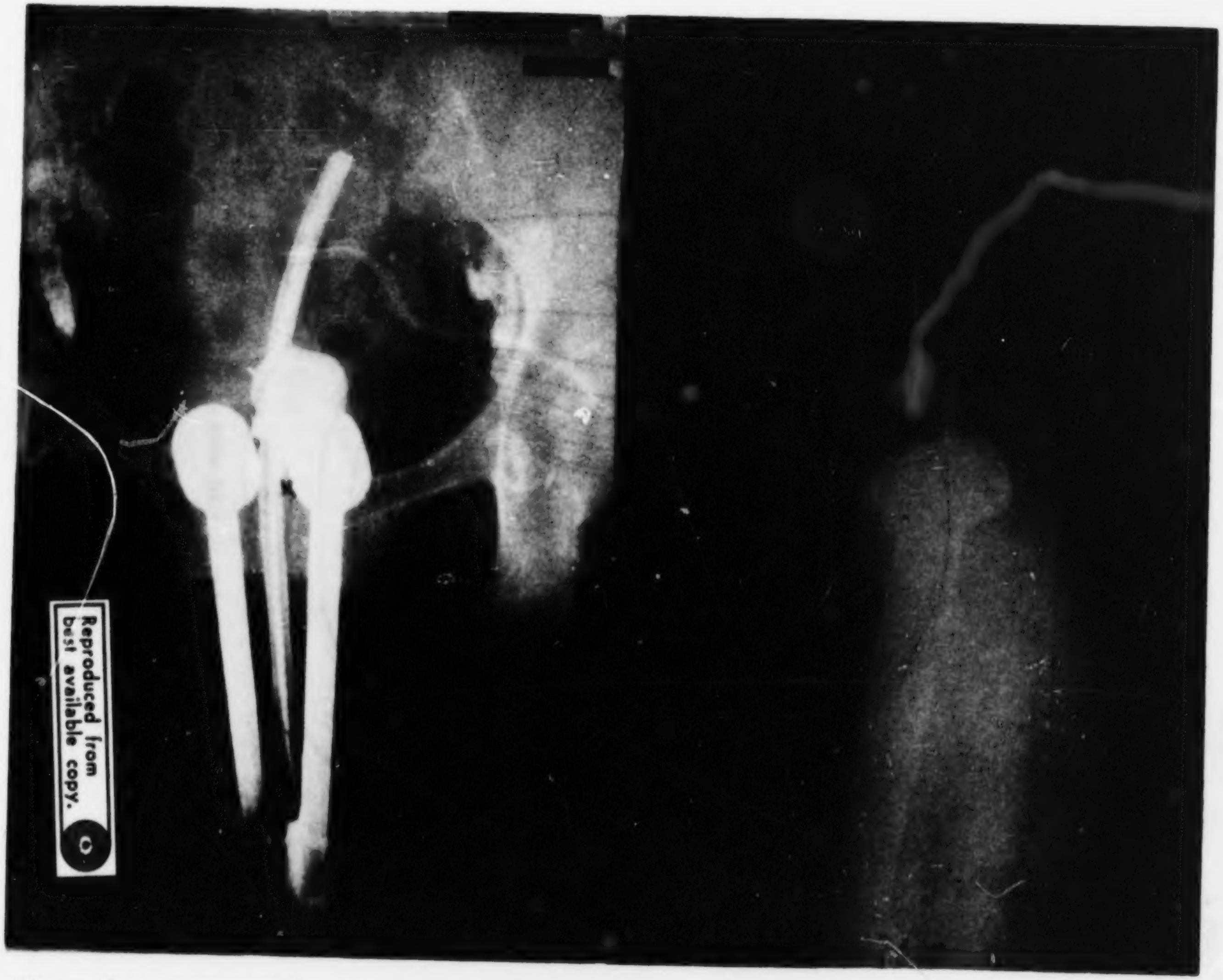

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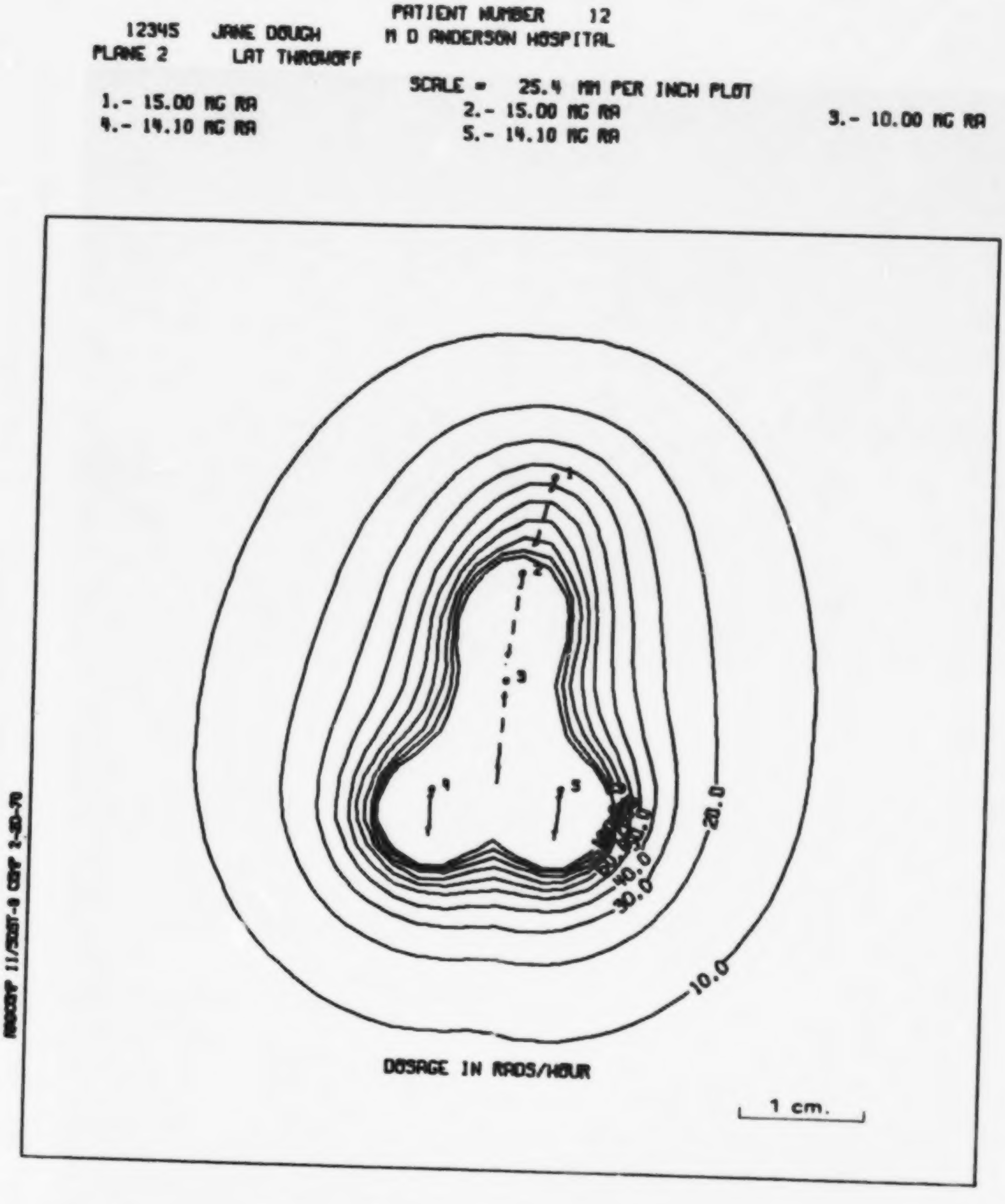
Figure 1a. Intracavitary therapy of the uterine cervix using radium in tandem and ovoids. Orthogonal radiographs (antero-posterior and lateral).



```
                              PATIENT NUMBER    12
     12345   JANE DOUGH      M D ANDERSON HOSPITAL
PLANE 2       LAT THROWOFF
                              SCALE =   25.4 MM PER INCH PLOT
 1.- 15.00 MG RA
 4.- 14.10 MG RA                  2.- 15.00 MG RA                    3.- 10.00 MG RA
                                  5.- 14.10 MG RA
```

Figure 1b. Intracavitary therapy of the uterine cervix using radium in tandem and ovoids. Dose distribution in a plane passing through the centers of the ovoids and the internal os.

PATIENT NUMBER 12
12345 JANE DOUGH M D ANDERSON HOSPITAL
PLANE 1 SAGITTAL PLANE
SCALE = 25.4 MM PER INCH PLOT
1.- 15.00 MG RA
2.- 15.00 MG RA
3.- 10.00 MG RA
4.- 14.10 MG RA
5.- 14.10 MG RA

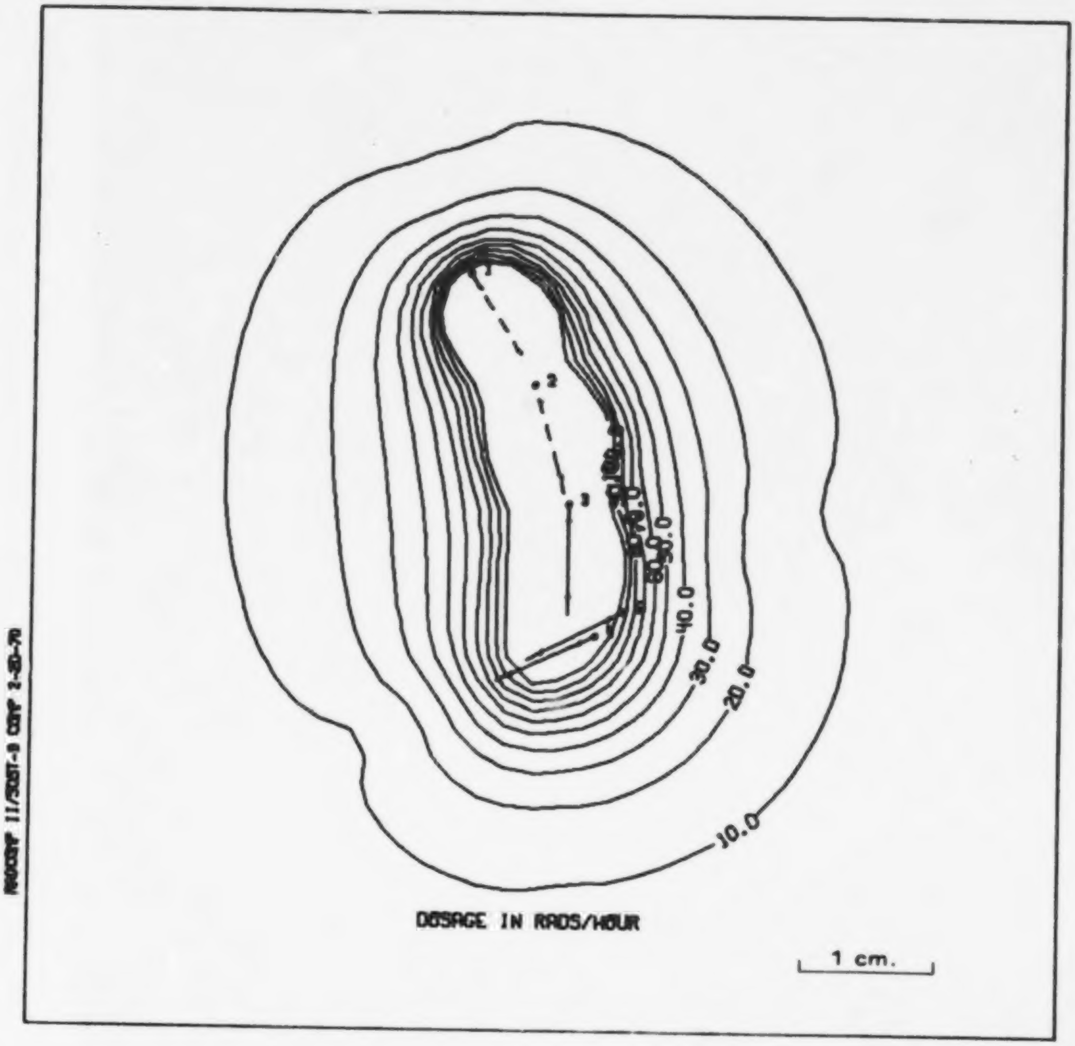


Figure 1c. Intracavitary therapy of the uterine cervix using radium in tandem and ovoids. Dose distribution in a sagittal plane passing through the tandem.

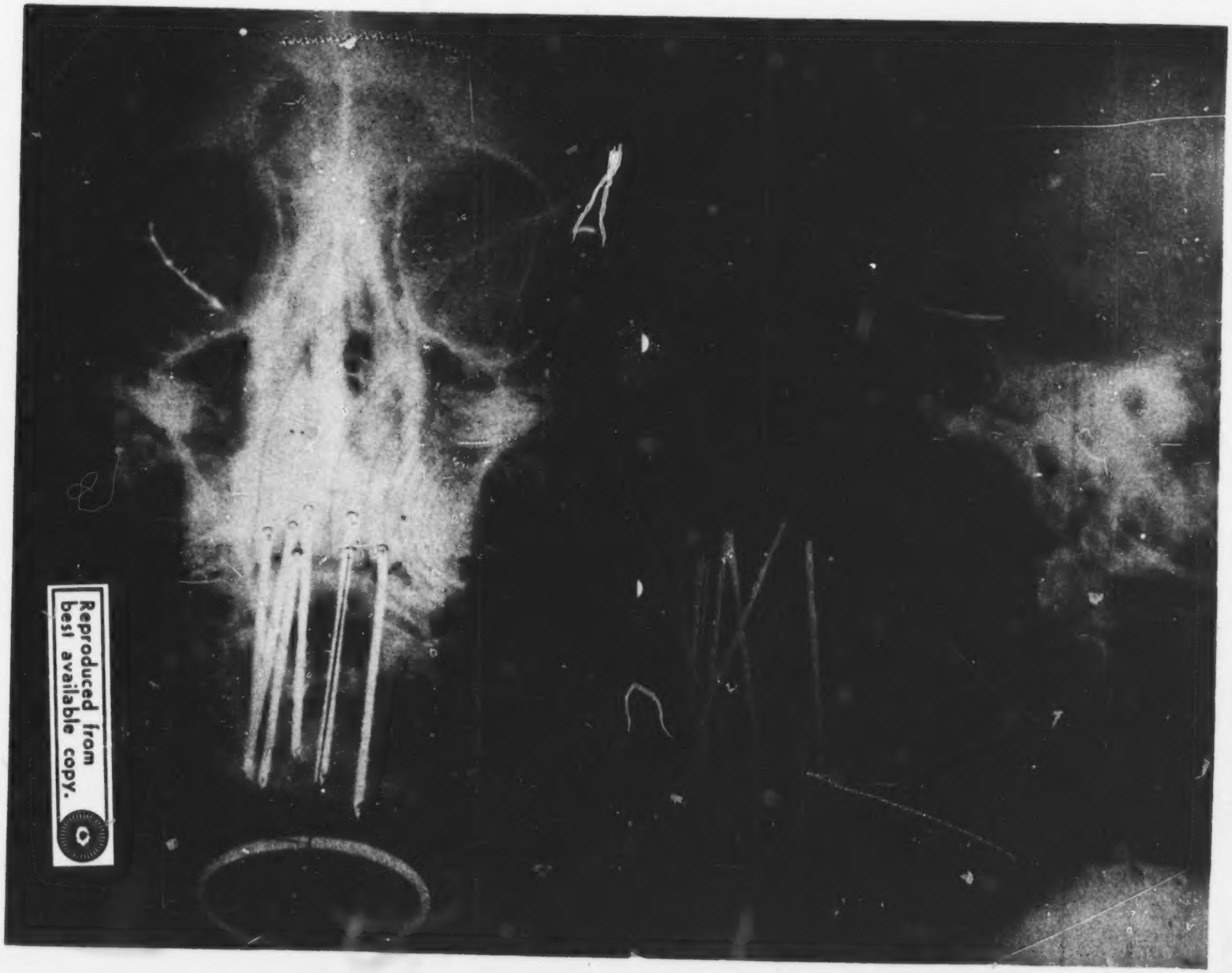


Figure 2a. Implant of radium needles to the floor of the mouth. Orthogonal radiographs (antero-posterior and lateral).

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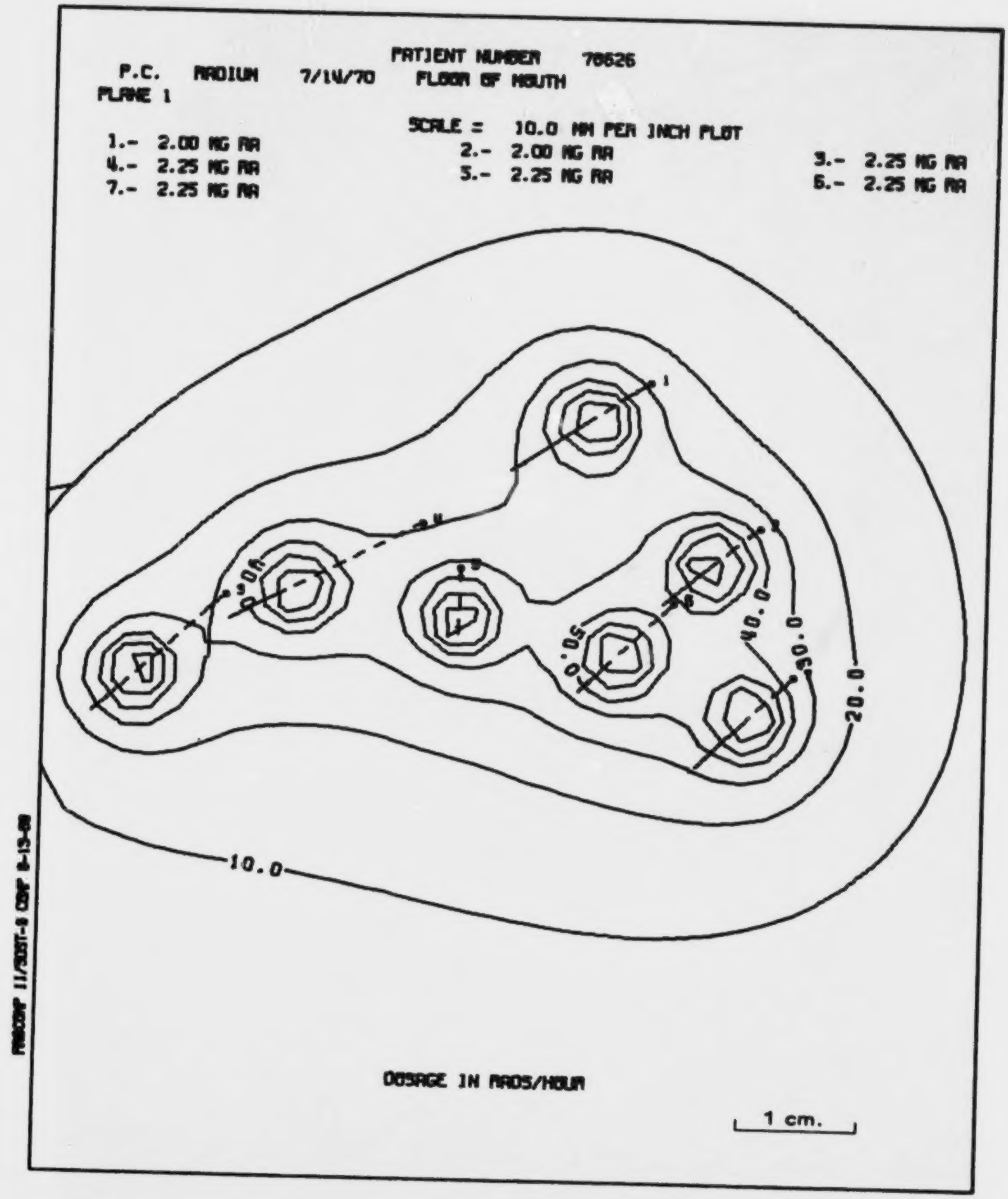

Figure 2b. Implant of radium needles to the floor of the mouth. Dose distribution in a plane passing through the centers of the needles.

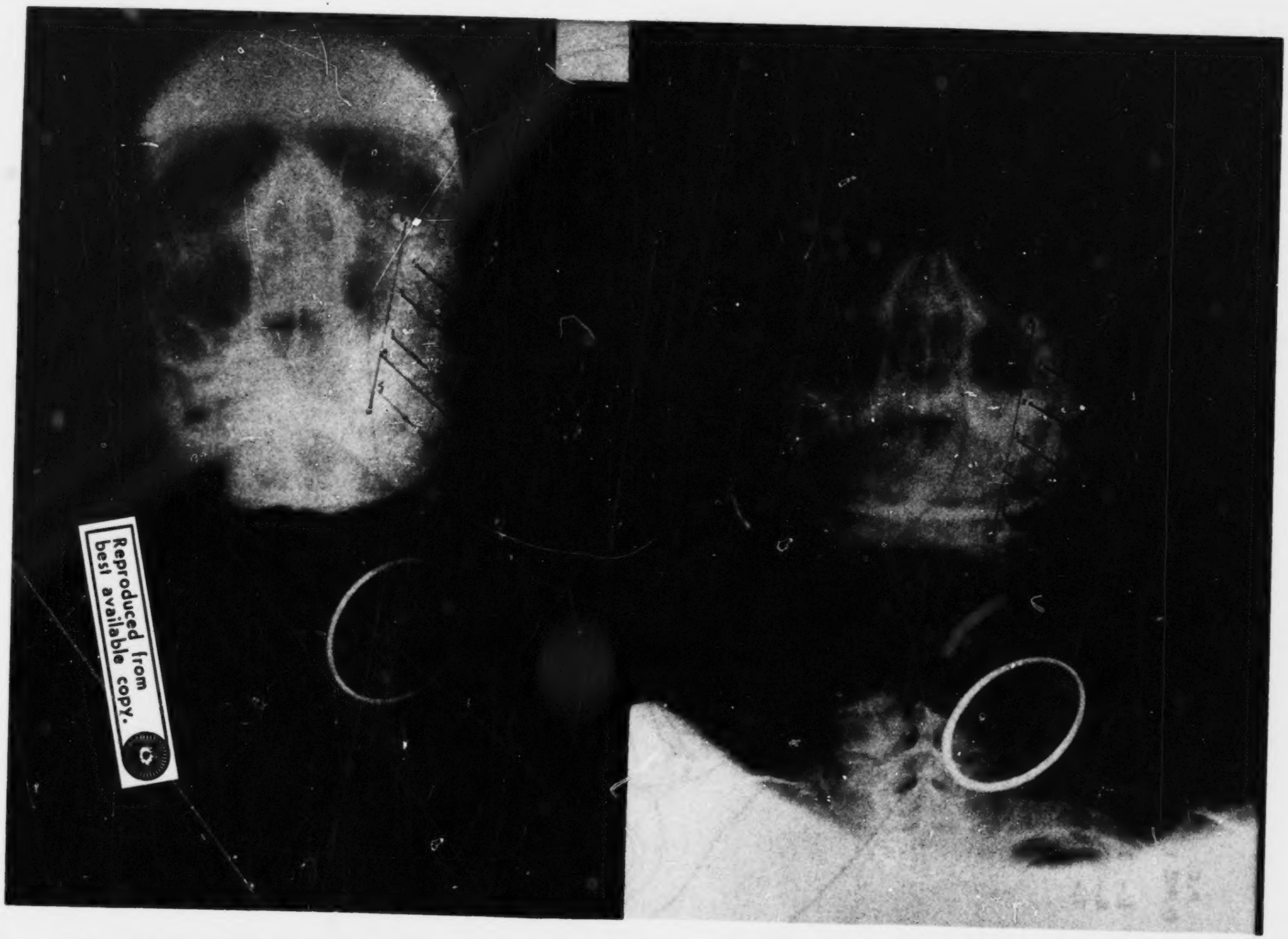

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Figure 3a. Implant of iridium 192 wires to the buccal mucosa. Stereographic radiographs.

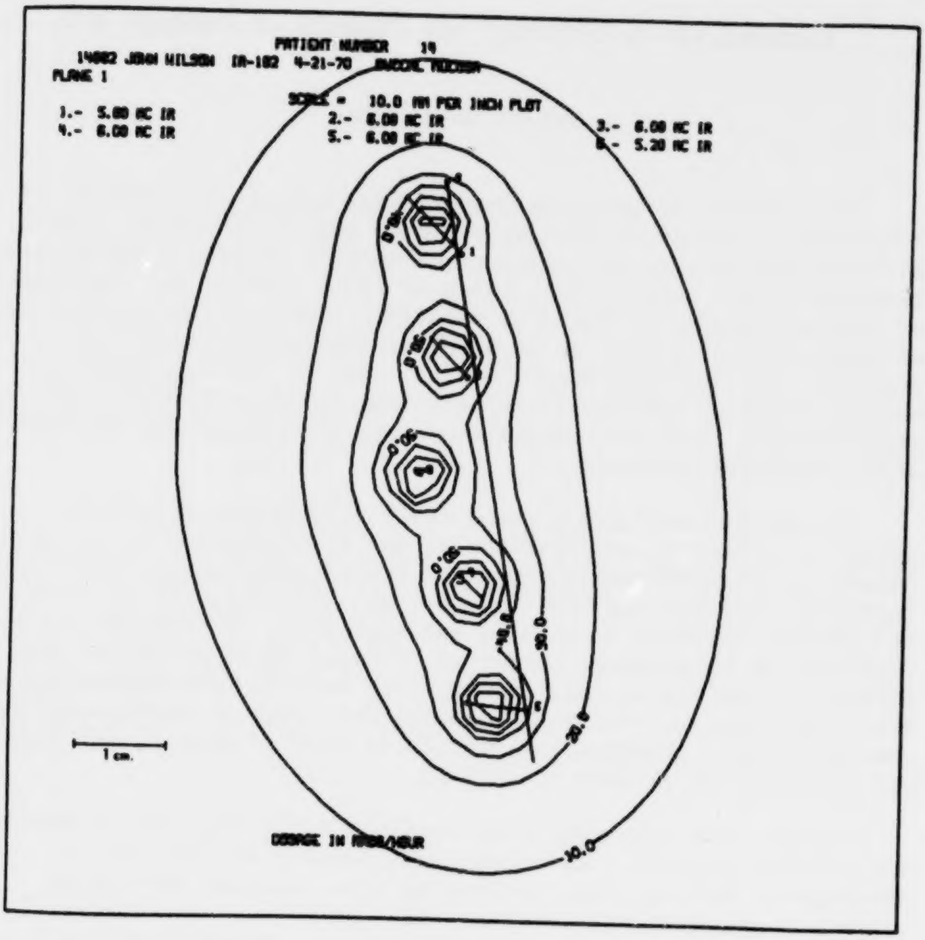

Figure 3b. Implant of iridium 192 wires to the buccal mucosa. Dose distribution in a plane passing through the centers of the five main wires.

AVAILABILITY OF COMPUTERS AND COMMENTS ON STANDARD USES

J. Garret Holt, B.S.

The utility of applying computerized methods to problems of dosimetry in radiation therapy has been well established. The earliest application of computerized methods to plan external beam treatment dates back to K.C. Tsien in 1954, then at the Department of Medical Physics at Memorial Hospital. The earliest application of computerized methods to problems of implant dosimetry are credited to Nelson and Muerk in 1956, then of the Department of Medical Physics. The early applications utilized limited computational models and the computations were limited by the capability of the existing hardware.

In the 15 years since these early attempts, a tremendous amount of effort by many workers in the field has led to the development of sophisticated programs. The development of computerized treatment planning capabilities has been aided greatly by advances in computer language as well as the tremendous advances in the capabilities of computer hardware. Present applications of computers to problems in radiation therapy include data reduction, dose time computations, treatment planning for internal sources and for external beams, teaching, automation of machine control and logging and retrieval of patient chart data.

Today, many hospitals have computer facilities for bookkeeping and billing purposes. The question generally arises: is it possible to utilize these accounting type machines for simple treatment planning calculations? The answer to this question is generally no. To take fullest advantage of computerized calculations, one should refrain from placing too many restrictions and constraints on the computational model and should aim for accuracy of computation, convenience of input and output, and rapid turnaround time.

It is possible to utilize a small programmable desk calculator, such as the Wang or the Hewlett-Packard, for data reduction, x-ray machine calibrations, dose time calculations, and perhaps simple radium insertions to a limited number of points, such as points A and B in BYN calculations. However, a fast dedicated computer with suitable peripherals or a large fast computer with a large amount of core storage is required for treatment planning. Generally the larger and faster the computer, the more economical the calculations.

Because of the high cost of software development for treatment planning, and the general unavailability of large computers in the past, the tremendous advantages of computerized treatment planning has not yet been fully realized. Some of these advantages are:

1. Accuracy of computation;
2. Possibility of detailed description of dose including three-dimensional distributations;
3. Capability of developing new and sophisticated treatment modalities for which dose distributions may be difficult or impossible to calculate manually;
4. Capability of optimizing a treatment plan by variation of the treatment parameters;
5. Ability to design detailed treatment plans for individual patients.

Today many institutions are interested in using computerized methods for treatment planning, and are wondering how one starts such a program. It must be stressed at once that computerized treatment planning does not take the place of good therapy, but rather lends support to good therapy. In addition, qualified physics support is still required. If these criteria can be met, there are several possibilities in getting started in computerized treatment planning.

The physical location of a large computer on-site no longer is a requirement. But if one were available, it is tempting to think of developing one's own program or to adapt someone else's program to this computer. The first is, at best, a rather costly duplication of effort; at worst, it results in a program that is inferior in capability and accuracy to those already in existence. The second is difficult and frequently results in a large, futile expenditure of time and effort. Three better courses are:

1. To purchase a small stand-alone treatment planning system;
2. To use a commercial time-sharing system for participation in a treatment planning network;
3. To transmit input data to a computation center by means of facsimile transmission.

Several small stand-alone treatment planning systems have been developed over the past few years. These systems consist of a small computer with associated peripherals that permit the user to rapidly digitize patients' data, perform treatment planning computations, display the results over a CRT, and finally produce a hard copy over some printout device. These systems are programmed in an interactive mode, the user communicates with the computer by means of a keyboard and analog device. Some treatment parameters are easily changeable and the resulting change in the radiation dose distribution may be displayed.

The original stand-alone treatment planning system, known as the Programmed Console (PC), was developed by Dr. Bill Cox and his associates at the Bio-Medical Computer Laboratory at the University of Missouri, in St. Louis, about 6 years ago. The PC was commercially built and marketed by Spiers, Inc. Since then two more modern versions of the PC have appeared on the market: the RAD-8, which is built around a PDP-8 computer and produced by DEC; and the PC-12, produced by Artronics. Basically, these three systems are the same and are capable of calculating dose distributions for simple treatments. All three systems accommodate dosage calculations for radium needle implants in one or more planes, and two-dimensional dosage calculations for external multiple port radiation beams up to 6 ports.

At the present time, none of these systems is capable of calculating dosage distributions from moving sources, or any other less conventional mode of external beam radiation therapy. The computation model for external beams in these systems is based on the superposition of isodose curves, requires having the appropriate isodose curves available. The utilization of these stand-alone treatment planning systems for treatment planning is rather simple and convenient, but the user is severely limited by their restricted capabilities.

Figure I shows a typical stand-alone treatment planning system consisting of processor, input keyboard, the display oscilloscope, the plotter and the positional transducer used for the digitization of input data. The cost of such a system depends somewhat on the peripherals chosen ,but is about $50,000.

The use of time-sharing opens up the possibility of communicating with a large computer for treatment planning purposes. Commercially available, it permits the user to dial the computer over ordinary telephone lines and to communicate with it by means of a terminal, usually a teletypewriter. Both input and output are transmitted and received via telephone lines by means of the terminal. Due to the nature of time-sharing, the computer appears to be exclusively available to the user, although in fact several dozen other users may be in simultaneous operation.

Two treatment planning systems are presently available over commercial time-sharing. One, developed by the Ontario Cancer Institute, is operating on the General Electric Medinet Time-Sharing Service. Copies of these programs are obtainable from the author, Dr. Jack Cunningham, and are available to any interested person. The authors assume no responsibility for the validity and maintenance of these programs, the applications are entirely left to the discretion of the users. Computer programs are available for the computation of dosage distribution from the interstitial/intracavitary application of high energy encapsulated sources, as well as for externally applied beams of cobalt 60 gamma radiation. Due to the limitation of the G.E. Medinet, tissue inhomogeneities are not corrected for. But the computations may be extended to moving sources, as well as irregularly-shaped fields.

A somewhat different concept in service is offered by Memorial Hospital through the Memorial Dose Distribution Computation Service (DDCS). The DDCS is a treatment planning network, and is specifically designed to fulfill the individual requirements of its members. Participation in the network is granted only to institutions that employ a full-time radiation therapist, and have adequate physics support in treatment planning. Access to the network is obtained by means of a remote terminal, usually a teletypewriter. The qualified user is assigned a number which identifies him for billing purposes.

The DDCS utilizes the time-sharing services of ITT (ITT Reactive Service), permitting the user to dial the ITT computer directly and perform his own treatment planning computations. There is no charge for participation in the DDCS, but the user is billed monthly by Memorial Hospital for the actual cost of his own computations. The ITT Reactive Service utilizes a fast computer with a large amount of core storage (360/65, 360/75), so the computational models are quite flexible. It is designed to accommodate all radiation patient parameters one is likely to encounter in radiation therapy. This includes dosage calculation for implanted encapsulated radionuclides of radium, radon, cobalt 60, iodine 125, etc., as well as all types of high energy external x-ray or gamma ray beams.

The user may supply his own data, which consists of TARs or TMRs and Off-Center Ratios, for an external beam. With these data, dose distributions within patients are generated by the program. The implant dosimetry programs are three-dimensional, and dosage planes may be generated at any orientation. The external beam treatment planning programs are two-dimensional, but encompass all known forms of radiation therapy, including tangential rotation, wedged fields, blocked fields, isocentric therapy and any number of stationary fields of different field sizes. Tissue inhomogeneities and patients' contours are taken into consideration in the calculations.

A time-sharing network such as the DDCS has many advantages. Providing the necessary security is maintained, it assures the contributing institution of complete control over its computer programs, and some control over their use. Any program released through the network is instantly available to all members of the group. The development of computer programs is stimulated, since feedback from the users is instantly available. Another advantage is the ability to display any of the users' files, which facilitate rapid troubleshooting and provides a means of assisting any user who experiences difficulties. Since time-sharing provides access to a computer by means of a remote terminal, it is possible to place these terminals in the most convenient locations. Finally, the operation of a group opens up the possibility to hold regular treatment planning workshops which would provide educational opportunities for the members of the group, and stimulate further development of the programs.

The major advantage has been the fact that the usual remote terminal, such as a teletypewriter, is limited to transmission speeds of 10-30 characters per second. In addition, the typewriter device restricts the output format to either a dose matrix or a dose contour map from which isodoses may be drawn manually. Although a dose matrix provides the most information, most users would prefer to see an isodose plot or a video display of the isodose curves.

Fortunately, it is now possible to offer this over time-sharing as well. A number of inexpensive plotters are available and are supported by the major time-sharing companies. The use of plotters removes the objection of the long printout time required. Figure 2 shows the application of a commercially available plotter, in conjunction with a teletypewriter. It is possible also to have a CRT display in addition to the plot. With the use of a suitable plotting device, printout time for treatment plans may be reduced by at least an order of magnitude. By having a complete treatment plan available within a matter of one or two minutes, it is practical to generate a number of alternative treatment plans for optimization or teaching purposes. Figures 3 and 4 show some dose distributions that have been generated by the DDCS.

There are presently over 3 dozen active members within the DDCS treatment planning network, and the number of computations performed is about 300 per month. Some of the collaborating institutions are utilizing the DDCS to perform treatment planning computations for smaller institutions within their Regional Medical Program.

The cost of computerized treatment planning varies according to complexities of the calculation. On the average, a dosage distribution for an interstitial/intracavitary implant is between \$5 - 10 per plane, and the cost of an internal beam calculation from \$15 to \$50 per treatment plan. In rare instances only is the upper limit exceeded, and then only at the option of the user.

Future developments in computerized treatment planning might include:

1. Use of a small stand-alone computer as an input terminal to a large time-sharing computer.
2. Use of a light pen type of input terminal to communicate with a large computer. One such effot is described here by Dr. Carol Newton.
3. Development of up-to-date computation models for small interactive systems to extend the capability of the stand-alone treatment planning systems.
4. Coordination of computerized treatment planning with radiation therapy automation.
5. Further development of three-dimensional computations, which critically depends on improved methods of data acquisition on the individual patient and three-dimensional data display.

In conclusion, one might ask the question: What effects has computerized treatment planning had on radiation therapy? Has it improved survival statistics? Has it lowered the cost per treatment? The answer to the first question is probably that it is too early to assess, the answer to the second question is probably no.

However, it may be said that the more sophisticated approach to dosimetry has opened the possibilities of developing more sophisticated modes of radiation therapy. The application of gravity-oriented rotating blocks are a good example of a very sophisticated mode of treatment made possible by the application of computer methods to dosimetry. Figure 5 shows the gravity-oriented blocks mounted on a telecobalt machine, and Figure 6 shows the resulting dose distribution obtained by a full rotation with the gravity-oriented blocks in place.

Another aspect of computerized treatment planning is the renewed emphasis on tumor localization. The accuracy of the computer generated dose distribution depends critically on an accurate knowledge of the location of the tumor and the body inhomogeneities. To this end, such sophisticated localization procedures as transverse horizontal tomography, density distribution scanning, and treatment simulation have been developed. These methods, and others, supply the radiologist with amore accurate knowledge of regions to be treated.

Patient localization is another area where rapid development is in progress. With the advance of automated radiation therapy departments, the reproducibility of daily prescriptions is the weakest link in the chain.

The effect of all of these developments on radiation therapy can only be assessed in the future.

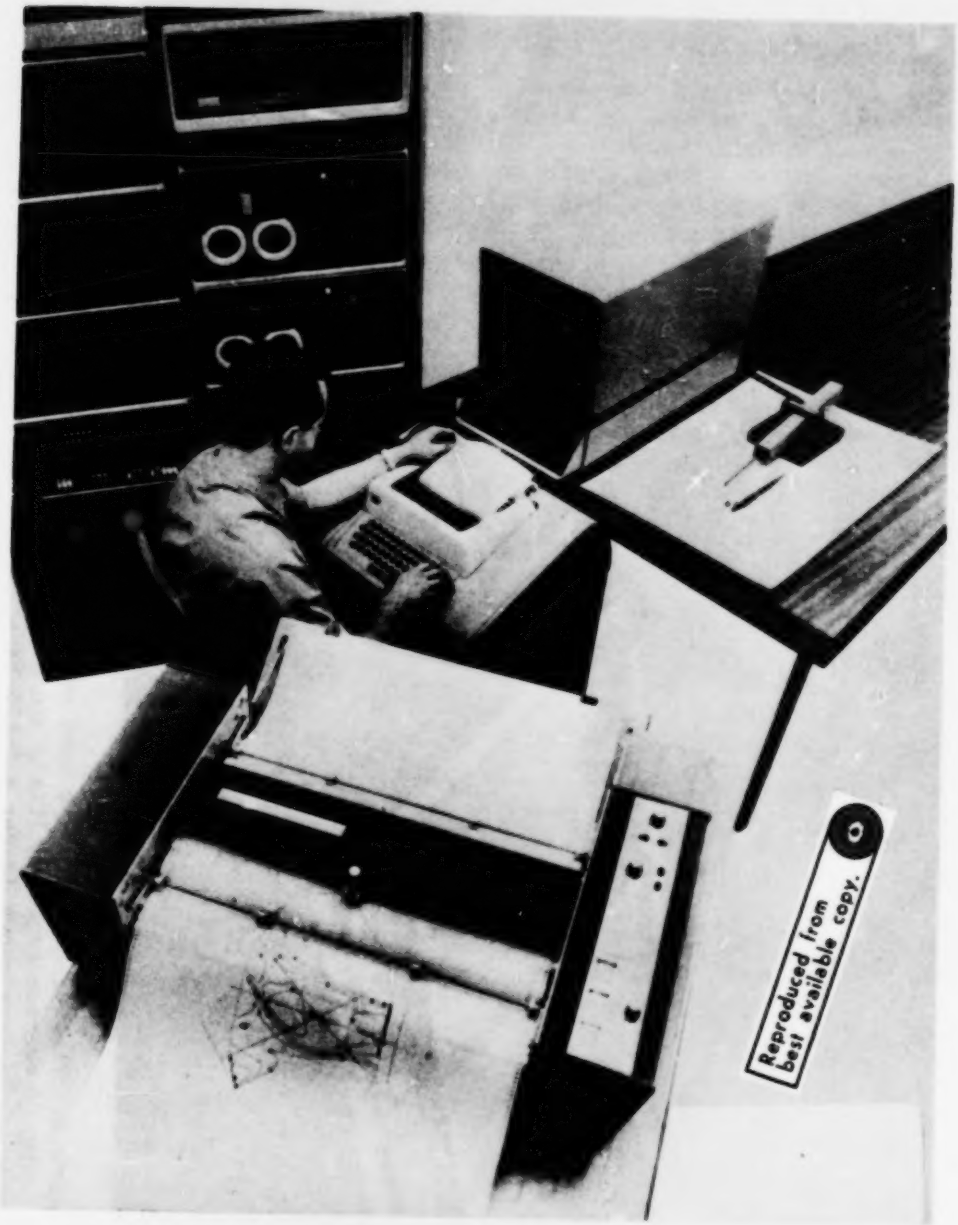

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Figure 1. Stand-alone treatment planning system consisting of processor, teletypewriter, display oscilloscope, plotter and positional transducer. Isodose curves may be displayed on the CRT and plotted. The system operates in an interactive mode, which is very convenient, but is limited in capability.

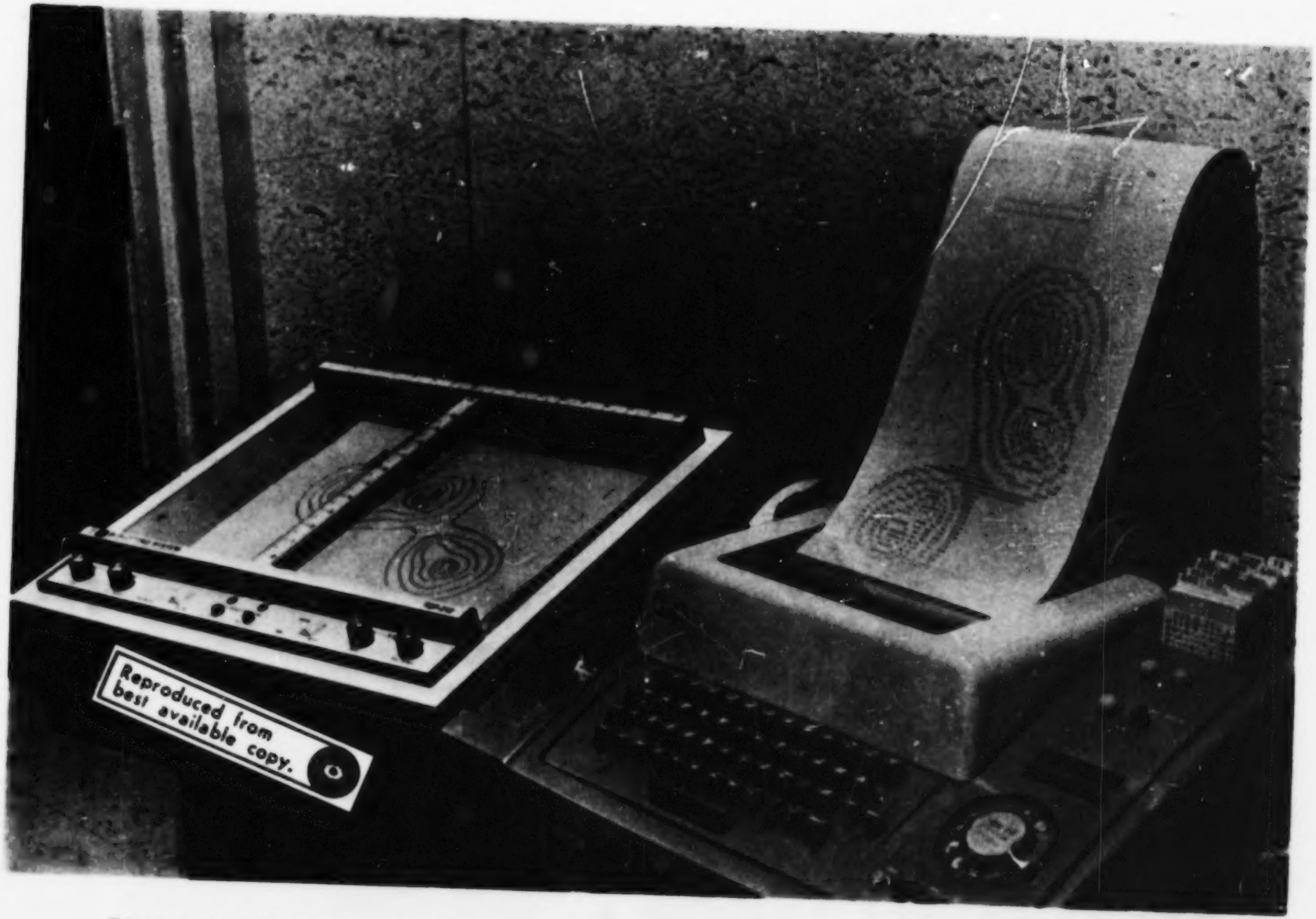

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Figure 2. Plotter and teletype used over time-sharing. Both map and isodose contour representations are possible using the MDDCS system. The output above is for a I-125 treatment of the entire right lung. This implant consisted of forty-nine I-125 sources.

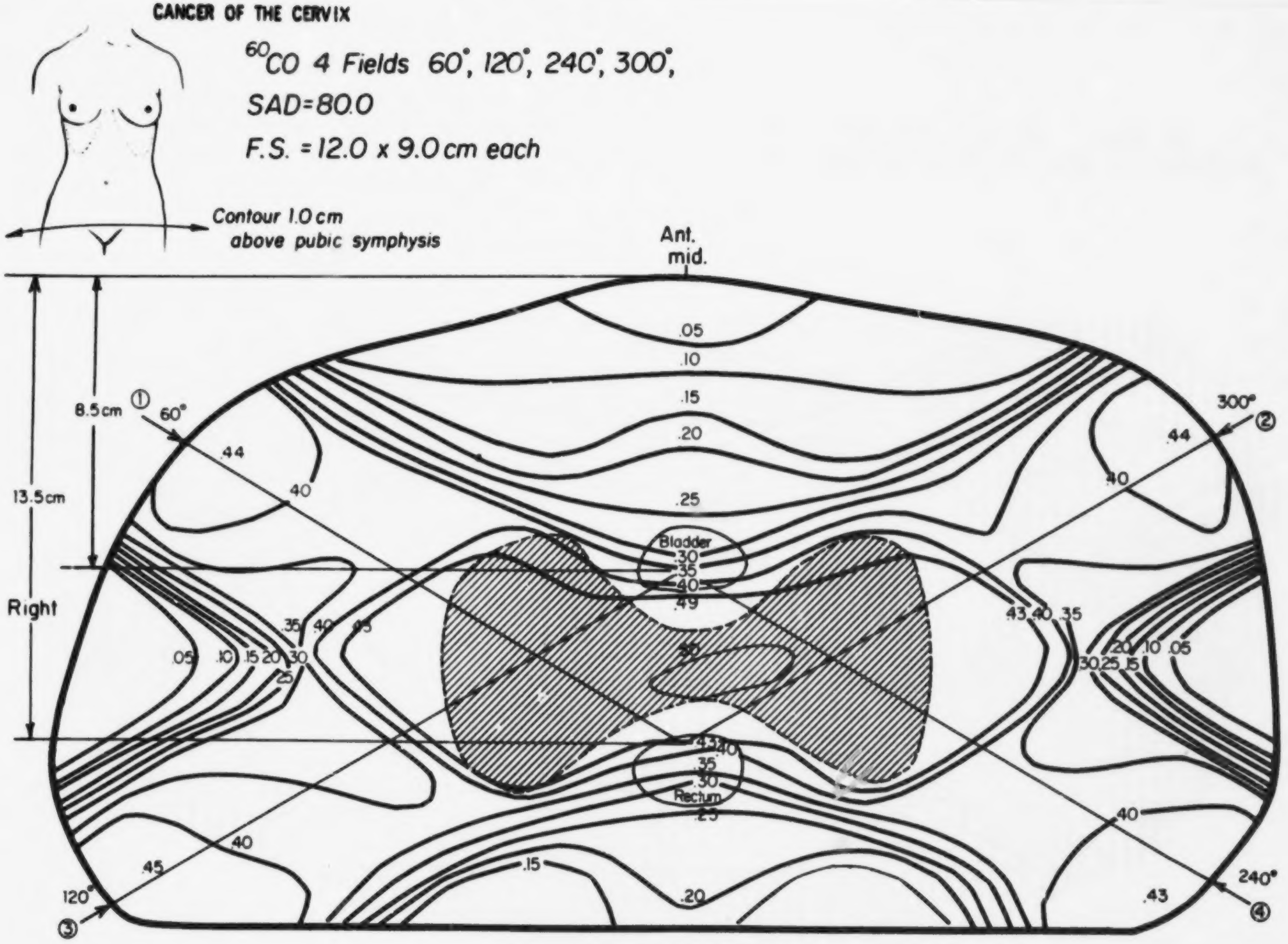
CANCER OF THE CERVIX
⁶⁰CO 4 Fields 60°, 120°, 240°, 300°,
SAD=80.0
F.S. = 12.0 x 9.0 cm each
Contour 1.0 cm above pubic symphysis
Ant. mid.
8.5 cm
13.5 cm
Right
① 60°
② 300°
③ 120°
④ 240°
.05
.10
.15
.20
.25
.30
.35
.40
.43
.44
.45
.49
.50
Bladder
Rectum

Figure 3. Cancer of the cervix treated with four fields of cobalt-60 gamma rays. The treatment plan was drawn from the computer generated dose contour map.

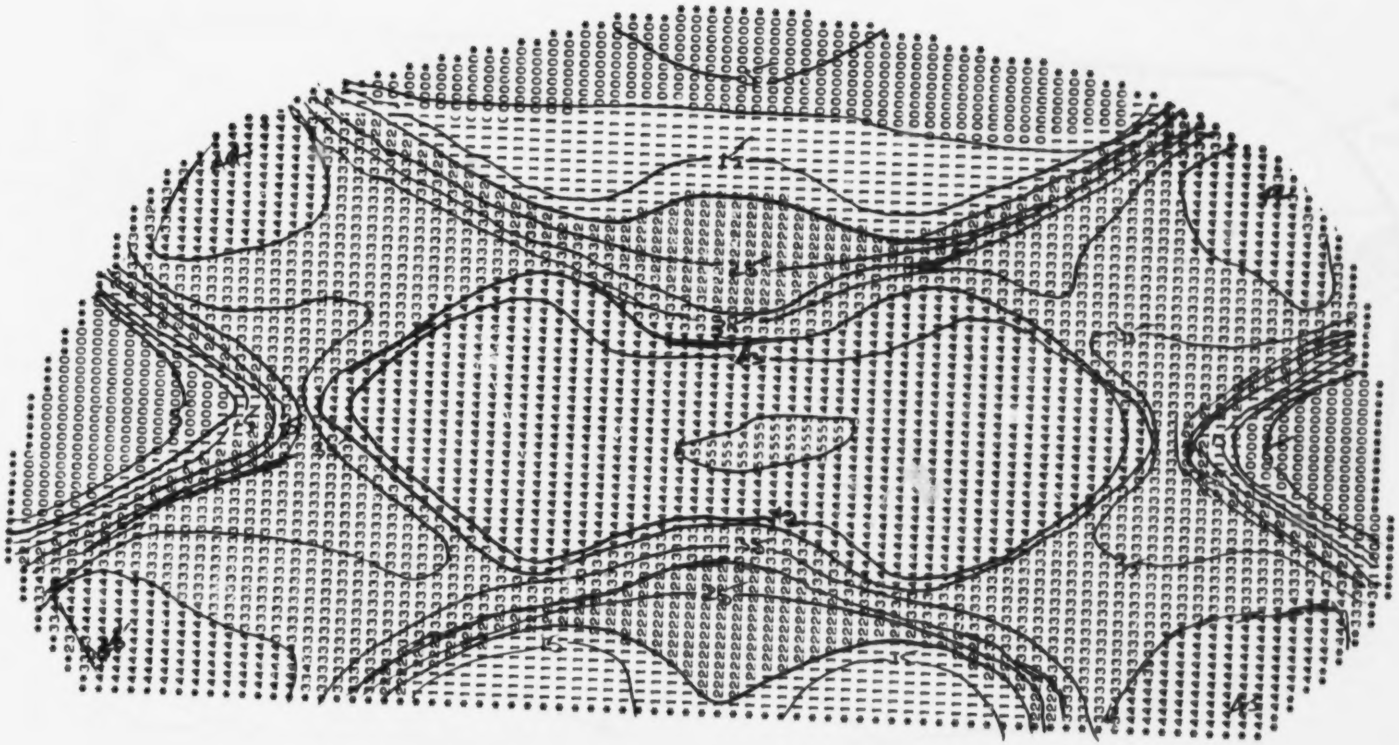

Figure 4. Computer output printed by a teletypewriter. The numbers represent 10% increment of dose levels. The treatment plan in figure 3 was drawn from this map. Cost of computation was $18.

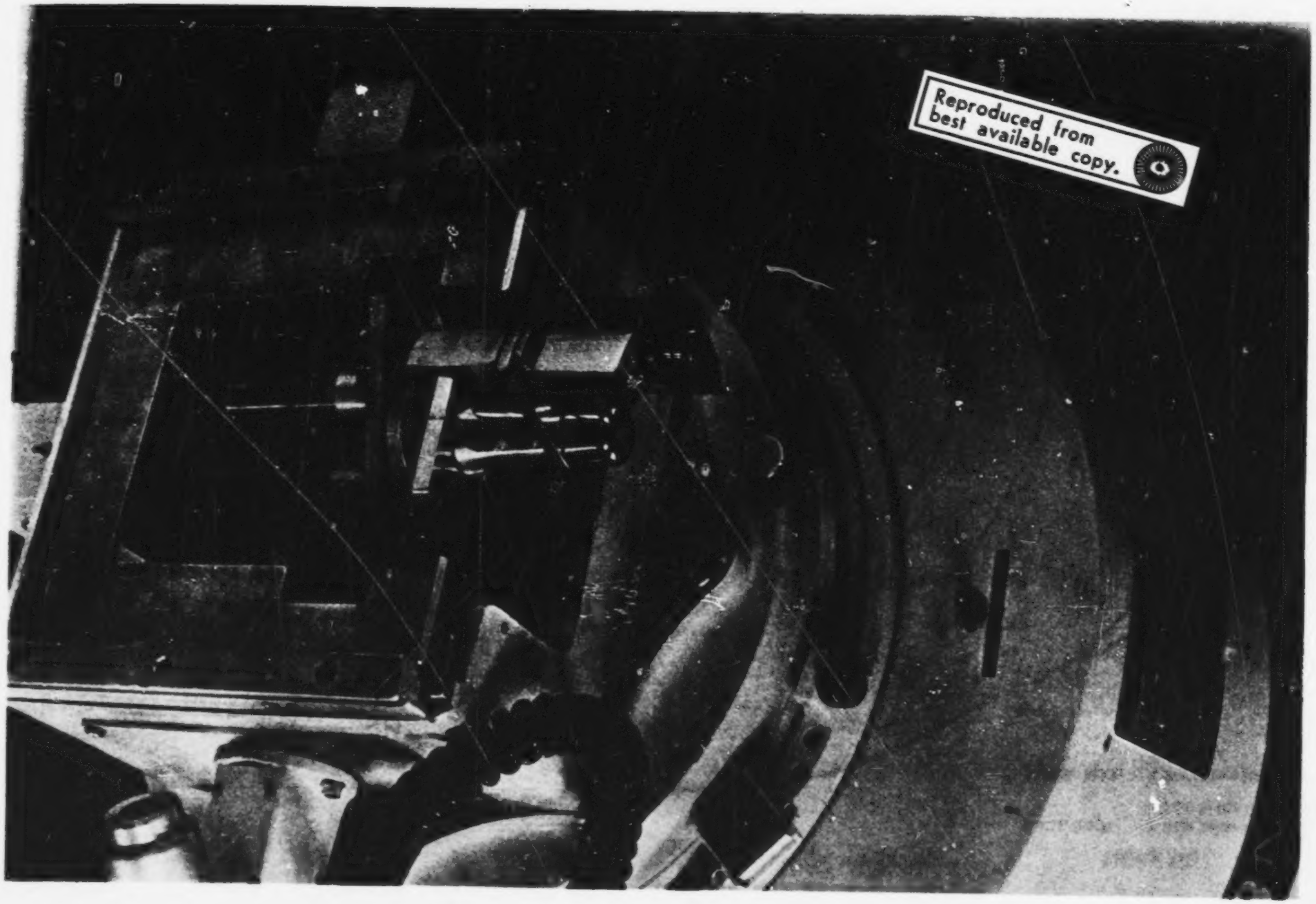

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Figure 5. Gravity-oriented beam blocking device (first developed by Proimos). As the cobalt-60 beam rotates about the patient, the orientation of the two lead cylinders, which are free to pivot about a horizontal axis, is kept constant by means of the weights at left. This results in specific radiation shielding to rectum and bladder.

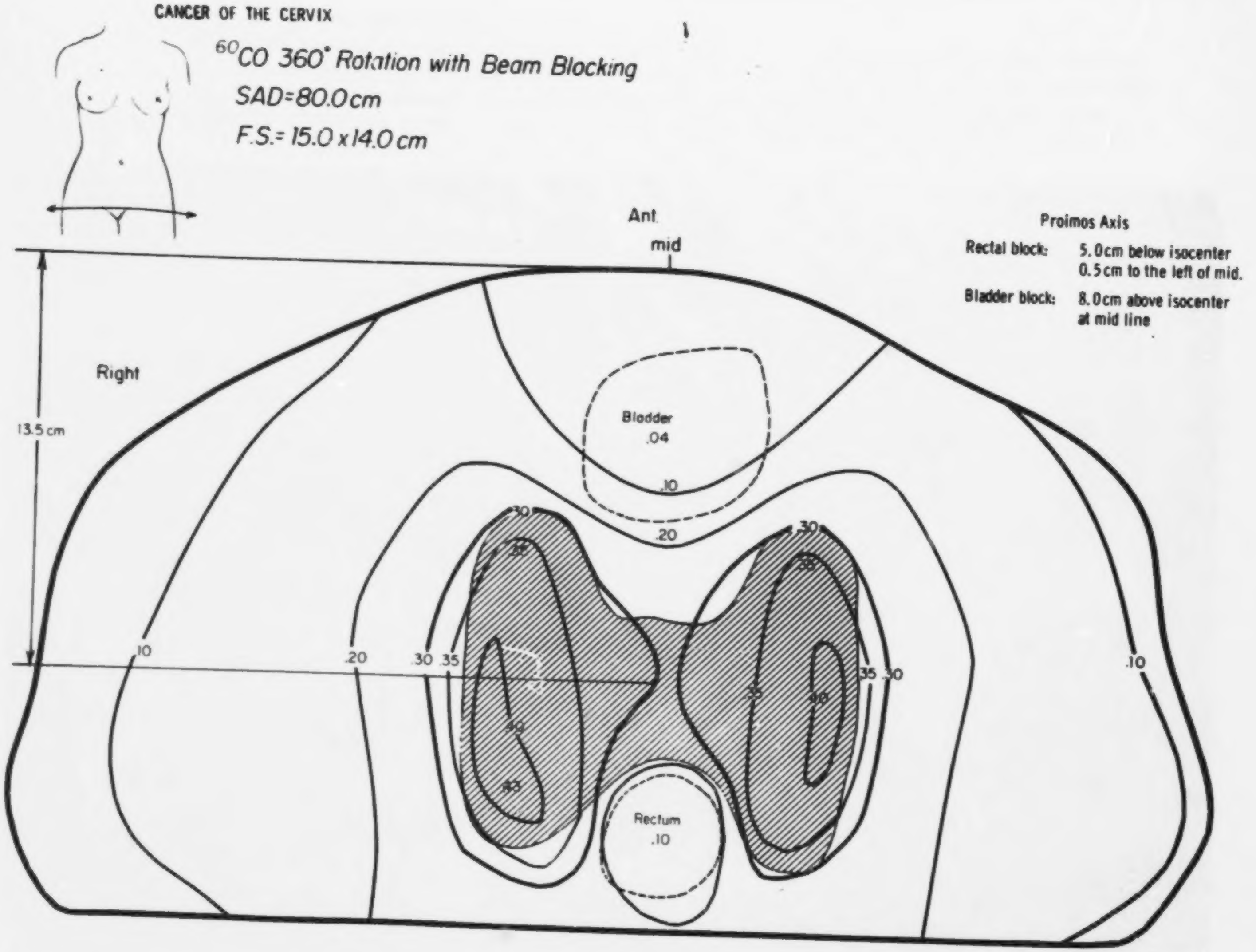
CANCER OF THE CERVIX
^{60}CO 360° Rotation with Beam Blocking
SAD=80.0cm
F.S.= 15.0 x 14.0 cm
Ant.
mid
Proimos Axis
Rectal block: 5.0cm below isocenter
0.5cm to the left of mid.
Bladder block: 8.0cm above isocenter
at mid line
Right
13.5 cm
Bladder
.04
.10
.20
.30
.38
.10
.20
.30 .35
.40
.43
.35
.40
35 .30
.10
Rectum
.10

Figure 6. Dose distribution resulting from the Proimos blocking device depicted in figure 5.

COMPUTER USE IN FRANCE

Andree Dutreix, Ph.D.

Radium has been used at the Institute Gustav-Roussy since 1921, as shown by certificates of activity of some of our sources. It is apparent that 50 years ago only elementary precautions were taken to avoid hazards.

The problem of contamination by radium daughters certainly is not new. Twenty years ago Frederic Joliot made an autoradiograph of a page written by Marie Curie, and you can see there the presence of radium, particularly at the place of a fingerprint (figure 1). Tubes and needles were not examined for leakage at our center until 1956. We were surprised to find that about one third of the total number of radium needles presented some leakage. No leakage was observed, however, in the radium tubes.

Checking all the tubes and needles in use was very difficult, since the total activity of all our tubes and needles amounted to more than 2 Curies. Before we could test every source, a serious accident occurred. An applicator used to treat hemangioma with beta rays emitted by radium broke, and we were obliged to decontaminate not only the storage area but the entire department. We checked the other applicators immediately, and all of them showed severe leakages.

Three new applicators were bought at that time, and only one year later these showed leakage. Decontamination of walls, floor, ceiling, lead screens, instrumentation and so on, was a terrible job. We decided to speed up the use of new radionuclides, in order to gradually eliminate radium sources.

Dr. Pierquin and Dr. Chassagne already had demonstrated the clinical advantages associated with the flexibility of the new materials. However, some of the radiotherapists of the Institute Gustav-Roussy were a little reluctant to use isotopes other than radium for therapy. They were afraid that the modifications in the shape of the sources and the lower energies of the gamma rays would introduce changes in the dose pattern. We had to make accurate comparisons of dose distributions for typical radium applications, and for applications with the new sources. Such calculations are so laborious, using conventional methods, that we decided to write a computer program to calculate doses around the sources. The results were tabulated in such fashion that it was possible to quickly draw, isodose lines. The Magnification was used to increase the accuracy of the drawings (figure 3).

These results were helpful, but isodose curves had to be drawn by hand and their size could not be determined directly due to magnification. When dealing with practical applications, however, any theoretical application could be easily computed. Determination of the exact coordinates of the source end-points was necessary, raising an additional problem. Neither the entry of the data nor the display of the results was satisfactory to the clinician. The physicists were very proud of their work, but it was not much appreciated by the therapists, so both of us were disappointed.

The display was much improved by the use of a curve plotter (figure 4), and we could begin an atlas of isodose sheets for parallel radioactive lines of various length and spacing. From these curves, thanks to the clinical experience of Bernard Pierquine, we could begin to establish the first rules of application for parallel wires.

The first program was written in 3 months. It took us 3 years to arrive at the present version, and we are not at all sure that it is the final one.

Once a week, radiotherapists and physicists examine the radiographs and isodose curves. They discuss physics and therapy. Starting from these discussions, modifications are introduced in the computer programs to meet clinical requirements. Two similar programs are used, one for interstitial therapy and the other for intracavitary applications. Both programs can be used for any isotope, for point sources, for needles as well as curved wires (figures 5, 6, 7). They take in account tissue attenuation.

Another program computes doses when filters are used, even with complex shapes such as the series of steel beads set between point cesium sources in the Curietron. Coordinates of the projections of the sources are read on two perpendicular films, irradiated in a special jig. It is not necessary to accurately know the positions of the x-ray source. Lead marks enable the computer to do necessary corrections. Data for anatomical and other points of interest can be read on the two films. Actual coordinates are automatically computed, taking into account divergence of the x-ray beam. The estimated error on these coordinates usually is less than 2 mm. It can be more critical on anatomical points which are not so easy to locate.

The main difficulty is the identification of sources on the two radiographs, particularly in interstitial therapy where many sources are used. In practice, this problem is more easily solved by the radiotherapist who has made the implant. So we always insist that he do the identification.

The results are presented as isodose curves drawn in any chosen plane. The choice of planes of interest is the responsibility of the clinicians. The specification of these planes is very simple, and relevant data can be determined easily by any medical resident. It seems to us very important to facilitate communication between computer and physicians.

Projection of sources in the plane of calculation, together with the intersection of sources with this plane, are shown on the isodose sheet. Projections of the anatomical points chosen as reference points are also represented. They are enlarged to the same size as the radiograph for sagittal and frontal planes. Thus it is possible to superimpose the isodose curves on the radiograph on a light-box. These anatomical references are also essential if one wants to add doses from external therapy to the doses from intracavitary therapy.

A computer program exists to add doses from external cobalt irradiation to cesium intracavitary applications. However, several problems raised by this program are not yet solved. The relative position of the anatomical references between the two irradiations always varies, and addition is not theoretically possible. Moreover, how can we add rads from fractionated irradiation to rads from continuous irradiation?

As usual the mathematical problems, even though especially complex, were much easier to solve than the clinical or biological.

Our programs were written in Fortan IV, thanks to a grant from D.G.R.S.T. in a joint contract with the Curie Foundation. They are available to any radiotherapist or physicist who asks for them. We offer help in adapting them to his own computer facilities, as we know by experience that this is a tremendous job for anyone who does not know the details of the program.

Our programs have been adapted to four computers from various manufacturers. Furthermore, a university computing center in Paris (Centre de Calcul de la Salpetriere, Pr. F. Gremy) is ready to compute doses immediately for any radiotherapist who asks for it. It charges only for computer time, which amounts to about $30 per patient for the four typical planes described by Dr. Chassagne. Calculations are performed routinely for 7 hospitals in France. Data and results are sent by ordinary mail.

Thus computers enable the radiotherapist, even if he is working far from a big center, to check the dose repartition for his own technique and to compare it with that of any other center. They do not solve clinical problems, but that was never their aim. Nevertheless, we are sure they can help to improve techniques, in the near future that will become as necessary a tool as dosimeters.

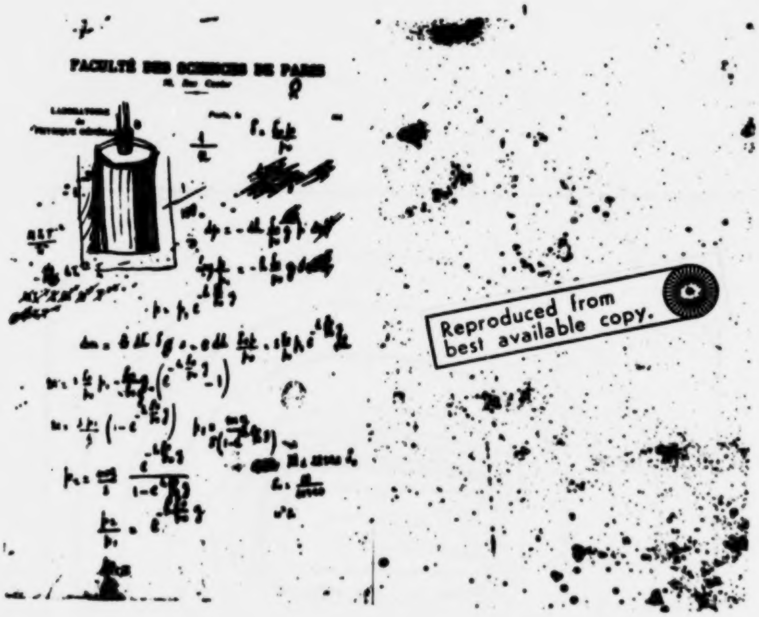
FACULTÉ DES SCIENCES DE PARIS

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Figure 1. Page of a notebook of Marie Curie with an autoradiograph showing the high radium contamination of the paper.
(Courtesy of Musee Curie, Institut du Radium, Paris)

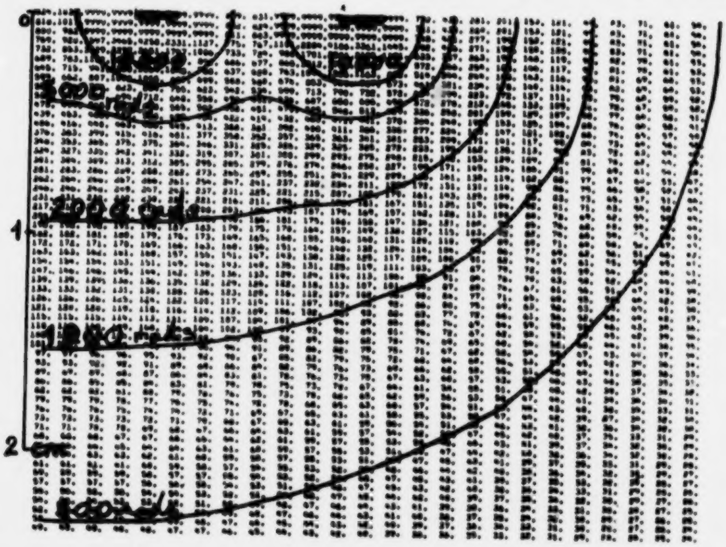

Figure 2. Doses are tabulated and isodoses drawn by hand

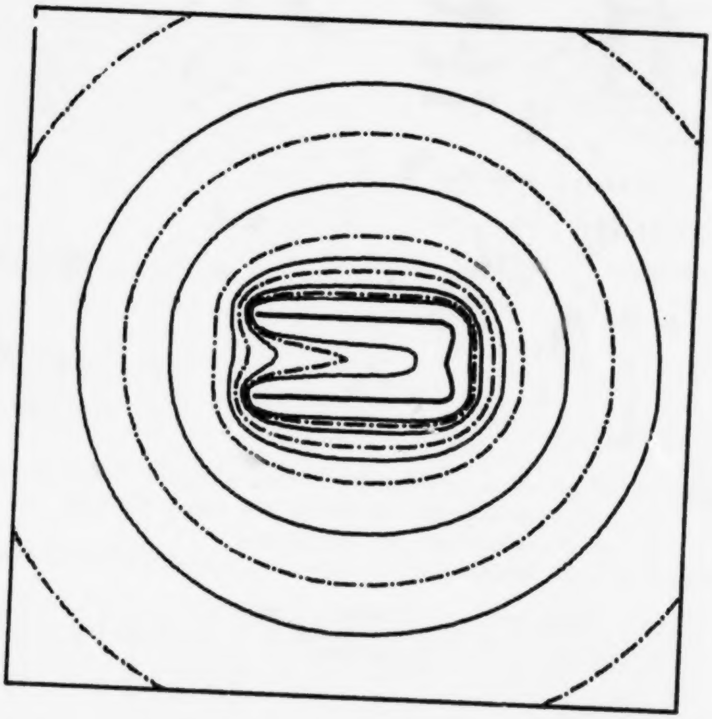

Figure 3. Isodose curves drawn by a curve plotter around an iridium hairpin. Linear activity is 1 mCi/cm. The curves correspond to dose rates from 1 rad/hour to 50 rads/hour.

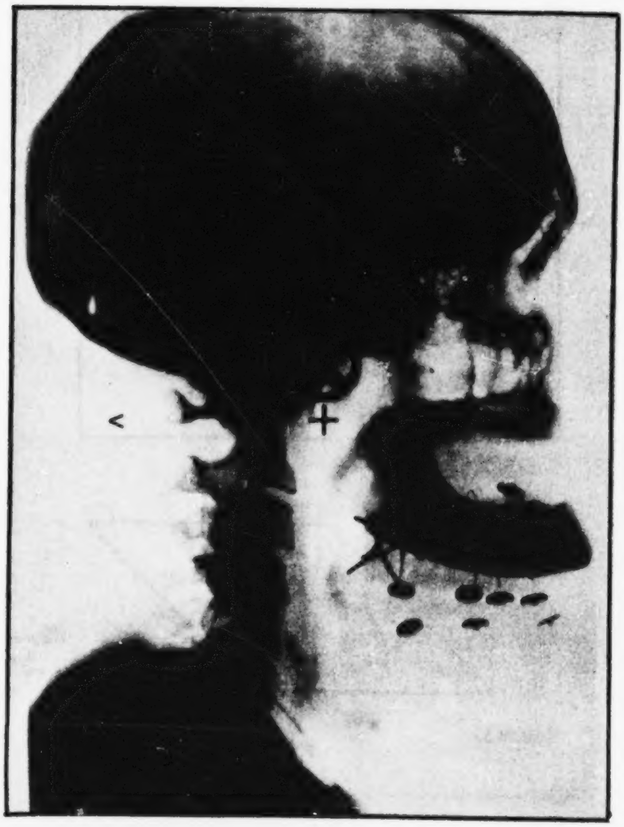

Figure 4. Lateral radiograph of a patient. Four iridium loops and one simple wire are implanted near the maxillary.

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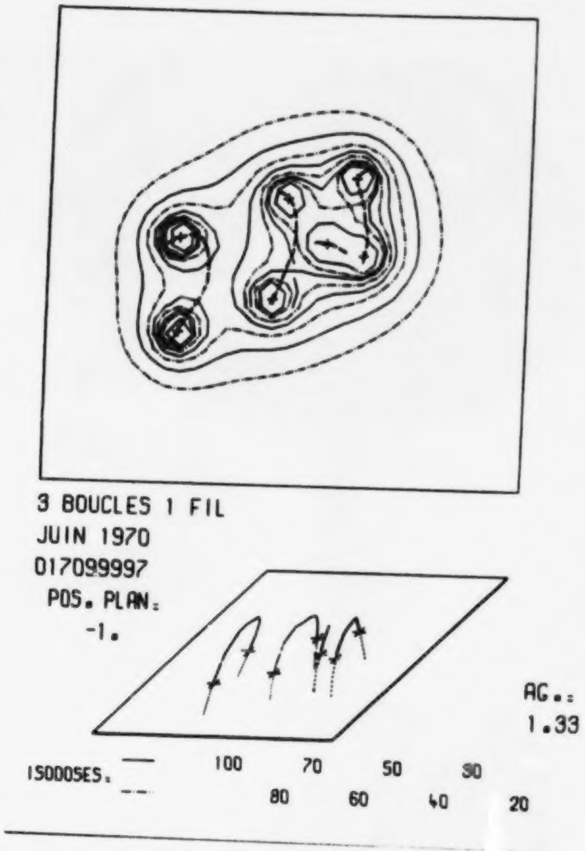

Figure 5. Isodose curves for the patient shown in figure 4. The plane of calculation is perpendicular to the wires (lower drawing). Dotted lines are projections of the wires.

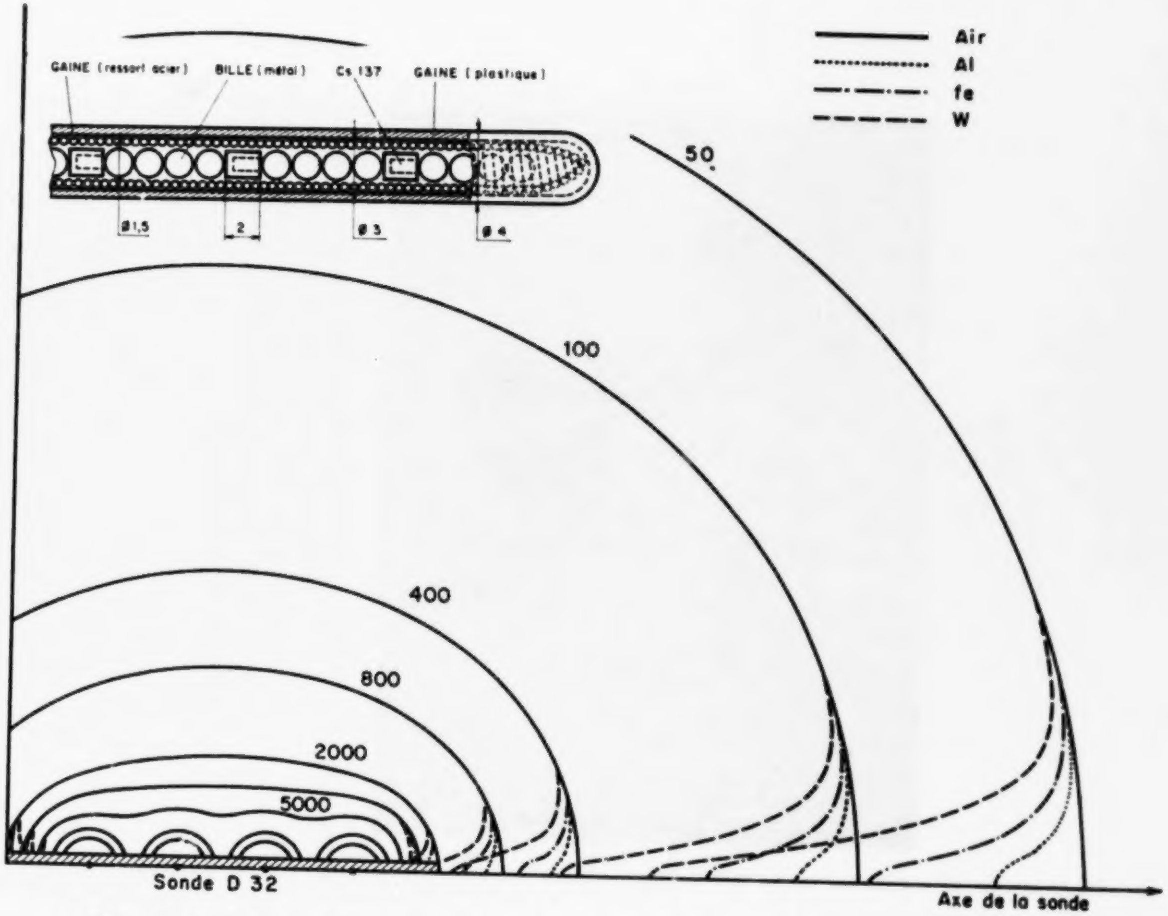

Figure 6. Isodose curves around a catheter with four cesium sources separated by inactive spheres. Calculation was performed for air, aluminum, iron, and tungsten. A section of the catheter is shown above.

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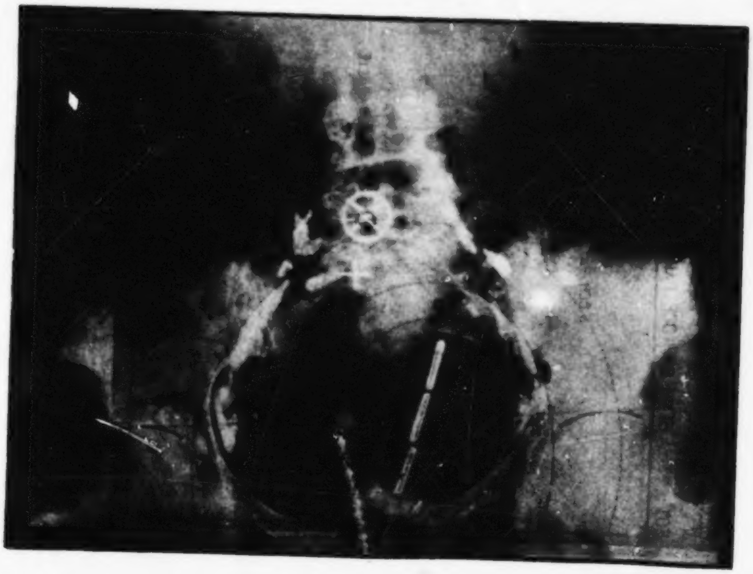

Figure 7. Isodoses calculated for gynecological application. Isodoses in the lymphatic plane are superimposed on the radiograph of the patient, showing good coincidence between lymph nodes and calculated points.

REMOTE GRAPHICS RADIOTHERAPY TREATMENT PLANNING[1]

Carol M. Newton, M.D., Ph.D.

I. REMOTE GRAPHICS RADIOTHERAPY TREATMENT PLANNING

It recently has become technically and economically possible to bring together two major areas in computer support to radiotherapy.

Programs developed by New York's Memorial Hospital, Houston's M. D. Anderson Hospital, and a number of other places have been tested and refined by years of practical use. In pioneering the remote delivery of such support to practicing radiotherapists, these centers have demonstrated clinical receptivity that has encouraged others like ourselves to invest seriously in program development. Program features such as three-dimensional computations required for implantation therapy, the treatment of tissue inhomogeneities, provisions for complex shielding, etc. require major computer support. Optimization programs and those suitable for new sources such as pion beams probably will demand even more.

On the other hand, enthusiastic acceptance of the Programmed Console developed by Cox and his associates at St. Louis has demonstrated the high value radiotherapists assign to an interactive graphics capability. This demonstration is all the more impressive when one considers the limited versatility and computational capacity of such equipment.

Until recently, we have had to choose between these two quite different, quite valuable types of computer support. This no longer is necessary. General-purpose interactive graphics terminals can now be purchased for less than $20,000. Those in which we are interested can operate over conventional telephone lines and be programed for modest local stand-alone computing, or to alleviate problems associated with low line-transmission rates. At present, the systems staff at UCLA's Health Sciences Computing Facility is writing a set of FORTRAN-callable GRAF subroutines for one of these terminals, the IMLAC PDS-1. Thus, graphics adaptation of existing, well-tested FORTRAN programs should not be difficult. Furthermore, users need know only FORTRAN to develop their own programs or modify those offered by others.

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[1] This research was supported by NIH Special Services Resources Grant RR-3.

Other rather obvious advantages follow when a graphics terminal is supported by a large computer. File systems usually are available to facilitate maintenance of relevant patient and treatment-center records. One hopes this will encourage the systematic documentation of treatment plans and outcomes which we need in evaluating new treatment techniques. To guide treatment of the individual patient, graphical summaries of blood-profile records, of summed dose distributions delivered to date, etc. should be helpful. Sophisticated programs for training residents in radiotherapy should result from all of the above.

Two problems must be considered. Most important is the limited transmission rate over conventional telephone lines. This problem should disappear if communications systems developed for television telephones become cost-effective, or if program development for clinical applications attains a level that persuades the United Nations to bring computer support to patients throughout the world by orbiting medical satellites. In the meanwhile, alleviation may be attempted by thoughtful designing of programs and utilization of the terminal's own computing capacity.

The second problem is that the more powerful, most economical machines for this work require preventive maintenance, and may unexpectedly go down for short periods of time. Unlike more emergent medical or surgical services, radiotherapy can tolerate these small delays. Nevertheless, it would be desirable for the same programs to be available from a number of computer centers.

One problem is not as serious as many suppose. People tend to overestimate both the magnitude and distance-dependence of telephone charges. It may not surprise you that on Saturday a 30-minute toll call from Los Angeles to San Francisco costs $7.50. However, an identical call to Boston or Washington costs only $6.10. On weekdays, corresponding daytime tolls are $10.55 and $13.50, falling at night to $7.50 for both.

II. RELATED WORK AT UCLA'S HEALTH SCIENCES COMPUTING FACILITY

Three aspects of our work at HSCF relate to remote graphics radiotherapy treatment planning. The possibility of graphical presentation has renewed interest in optimization programs developed several years ago. Practical interactive programs are being developed for external-beam therapy, and some approaches to intracavitary therapy. Systems support for remote graphics is one of the important aspects of this facility's basic program to further biostatistical research.

A. Treatment Optimization

It is doubtful that busy radiotherapists would intrinsically prefer trial-and-error treatment planning to automated optimization. Several optimization programs are known to exist, and Hope and Orr's program (1) is being used regularly in a few hospitals. Is cost the primary factor impeding acceptance? I suspect not. It seems more likely that people with direct responsibility for patient care are going to be reluctant to accept such programs until reliability has been demonstrated to their satisfaction. A mathematical demonstration may not suffice.

Furthermore, perceptive clinical feedback is required to define what optimality is in different treatment situations. Interactive graphics supported by a powerful processor provides both the analytical capacity and the pictorial representations required to support collaboration of theoreticians and practical radiotherapists.

Accordingly, there is renewed interest in work, first reported in 1968 (2, 3), on optimal withdrawal times for implants. Whether one inserts needles, seeds, or afterloaders, the desired source distribution frequently is not achieved. Corrective measures include adding sources or removing some earlier than others. The need to add can be assessed if one knows the best outcome realizable from different withdrawal times of the sources currently in place. If one seeks to reduce hot and cold spots by minimizing

$$\sum_i \left(\frac{D_i}{\overline{D}} - 1 \right)^2$$

where D_i is the dose delivered to the i-th point and $\overline{D}$ is the average dose for all points considered, it turns out that an exact expression is obtained for two or three different relative withdrawal times.

Interactive approaches have been tremendously helpful in exploring various algorithms for selecting which implants to withdraw first, for investigating the dependency of solutions on precise definition of tumor boundaries, and for devising sampling procedures for selecting the points to be calculated. Figure 1 shows an IBM 2250 graphics display for an economical, two-dimensional program for testing some of these algorithms.[2] Letters superimposed on the grid indicate the location of point sources whose relative strengths are indicated in the left hand column. It is assumed that there will be only two different withdrawal times, and sources selected for early withdrawal are brightened on the display.

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[2] The figures referenced in this paper were presented as slides and were not available in a form suitable for reproduction.

Figure 2 compares dose distribution for simultaneous removal of all sources to the case where there is removal at two relative times, as indicated by the optimization procedure. Bars on the two dose-volume histograms on the right represent the volume of tissue receiving doses in a specified percentage range relative to the mean dose delivered to the entire volume. Given that lowest doses are on the left, and that the lower histogram is for optimal withdrawal times,.it is immediately obvious that at least cold spots are being reduced by this procedure. It can be shown that there is a corresponding reduction of hot spots not immediately associated with a given source.

The number beneath the histograms represents the time for early removal, relative to that for removal of the remainder of the source sources. Dose-distribution plots on the other display (Figure 2a) identify areas receiving doses below or in excess of a specified percent departure from average dose. In the former areas, "C"s are plotted; in the latter, "H"s. Compared to the plot on the right which obtains for the two specified withdrawal times, that on the left (for simultaneous withdrawals) shows a greater area of overdosing near the clump of sources and more undertreatment on the periphery.

Figure 3 plots dose distributions for one plane through a three-dimensional array of interstitial needle implants. The one for simultaneous withdrawal is depicted on the left, that for three different withdrawal times is on the right. Here the plotted numbers indicate dose level. Central blank areas exceed twice the average dose; peripheral blank band indicates areas receiving the average dose. Note the reduction of central hot areas and peripheral cold areas by optimal withdrawals.

These approaches cannot be meaningfully accepted until practical radiotherapists have an opportunity to compare the treatment strategies offered by the program with the best measures they themselves can suggest. Graphical comparisons of competing treatment plans are more convincing than mathematical demonstrations. With remote graphics radiotherapy treatment-planning support, optimization procedures such as this can be subjected to the challenges that eventually will promote improvements and establish for them a place in standard treatment procedures.

Afterloading techniques are particularly suited to the optimization program described above, as geometries are not disrupted by the early removal of some sources.

B. Practical Graphics Program for Treatment Planning

These programs are being developed in collaboration with Dr.

Richard Nelson at the City of Hope.

At present, our primary emphasis is on the development of convenient data-input and meaningful dose-distribution graphical display programs. For the basic calculations, we would prefer at present to use well tested and widely accepted programs, such as those provided by Memorial or M. D. Anderson.

At this time, all of the interactive input routines that interface to the City of Hope's adaptation of Memorial's external-beam program are working. An isodose display has just been completed, and should be interfaced to the program by the end of next week. Although tablets or rho-theta devices probably would be more convenient, we have encountered no difficulty in tracing organ and body contours with the terminal's light-pen (figure 4). The other devices may be obtained at extra cost for the inexpensive remote terminal to which this work should be transferred by July.

At present, only the Fletcher system for intracavitary treatment is being programed. Suggestions concerning the relative importance of alternate approaches are especially welcome. The program maintains a brief file of patient information, and an inventory of available applicators and sources. Advantage is taken of known source geometry to simplify or verify input procedures. Isodose plots may be requested in any A-P, lateral, or transverse plane. The user may weigh economy and quality in specifying subdivision of each source for summating its contribution to a field point. We have postponed inclusion of the colpostat tungsten filters, as an x-ray inspection of one set did not confirm prior expectations of their geometry. We also have been informed that some filters now are manufactured from lead rather than tungsten. Until this is resolved, conservatism dictates that we set aside expectations of the filter's protection of rectum and bladder. Again, we would prefer to use well tested programs for basic dose calculations.

All possible advantage is taken of known applicator geometries in intracavitary treatment planning, and dialogue is designed to facilitate use by radiotherapists who are unfamiliar with more conventional computer inputs. In response to requests, at the bottom of the display the radiotherapist has indicated on an A-P view the location of features shown in the display in figure 5. He now is being asked to specify a length, tandem base to os. Given A-P location of tandem tip, base, and position at os, the program can uniquely locate the tandem in three-dimensional space, with possibly the need for additional information that the tandem tip is anterioflexed. Figure 6 shows the final A-P tandem projection; source loading of the tandem was accomplished previously.

Graphical display techniques such as those described at the end of Section II-A are being explored for economy and meaningfulness to the radiotherapist. Those shown in association with the two-dimension optimization program (figure 2) would transmit relatively rapidly over telephone lines. Isodose plots are available as well.

C. Supporting Systems Research

The systems staff that developed GRAF, FORTRAN-callable subroutines for the IBM 2250, is writing a similar set for the IMLAC. It is hoped that programs presently developed for the 2250 can be transferred to the IMLAC by this July. With this capability, it is convenient to interface existing FORTRAN programs to remote interactive graphics displays. It is anticipated that criticisms and suggestions from remote users will greatly strengthen interactive program development for practical radiotherapy.

A tandem consulting capability now exists for the IBM 2260 terminal users. A statistical consultant and his client can communicate with each other while alternating control of the program. Similar systems are planned for HSCF remote terminals. Both instruction in program use and users' suggestions for program improvement for certain cases can be communicated effectively in this manner. Thus a new dimension can be added to program exportation.

III. CONCLUSION

For increasingly sophisticated treatment techniques, increasingly sophisticated treatment planning probably will be required. Visually-guided hands-on exploration of treatment alternatives has found great favor with users of the Programmed Console. Now relatively inexpensive, telephone-remotable graphics terminals enable versatile interaction while providing the type of major computational support required for three-dimensional computations, complex shielding, inclusion of body inhomogenieties, or optimization. Radiotherapists using such terminals need not reside near large computer centers.

A revived interest in optimizing implant withdrawal times now is being directed to uterine intracavitary treatment planning. Practical remote graphics programs are being developed for this and for external-beam therapy. Strong systems support for this type of work is a consequence of HSCF's developmental program in systems supportive to modern statistical research, which has many similar requirements.

In the future, ways must be found to alleviate limitations imposed by slow transmission rates via conventional telephone lines. When the number and quality of proven supports to clinical practice warrant it, the United Nations should explore ways to make available to patients throughout the world medical-support programs developed in the various countries.

Improvements in the terminals themselves might include low-cost provisions for graded brightening, locally implemented array rotation, and a passive color monitor that facilitates distinction of organ outlines, beam specifications, and dose-distribution contours.

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THE PLACE OF COMPUTER DRIVEN DISPLAYS IN AFTERLOADING TECHNIQUES

Gordon Jameson, M.A., M.Sc.

I shall try here to provide the answer to a number of questions that must be in the minds of radiotherapists confronted with the possibility of using computers to back up afterloading techniques.

The first and most obvious question is why use a computer at all. The answer is, technical developments of recent years require their use if the dosimetry is to be meaningful, and if the clinician places any value on accurate dosimetry. The two principal developments are:

(1) The use of wire or seed sources for implantation, such as iridium 192. The wire is flexible and one of its virtues is that it can conform to the patient's anatomy in a way that rigid needles cannot. Since the wire does take up irregular shapes, however, the dose contributions are more difficult to ascertain. One way to overcome this is to consider the length of wire to be made up of a number of straight segments.

(2) The use of small sources 1-2 mm in diameter and a mm long. These are now available using cesium 137. They are small enough so that in intracavitary insertions a number may be used to fill the cavity. Again we are using relatively large numbers of sources, which indicates the use of computers for dose computations.

Where standardized techniques such as the Manchester System are used for cancer of cervix uteri, computer dosimetry probably is required only at the request of the radiotherapist. One result of the present trend in afterloading techniques is to introduce more individualized treatments, and here computer dose control is important.

In general, the use of computers in radiotherapy falls into three main groups:

(1) Centers using small dedicated computers such as the Programmed Console, or the PDP 8 system developed at Royal Mardsen Hospital in the United Kingdom;

(2) Centers using either a central computer in the batch mode, or timesharing systems over distant telephone lines.

There is, of course, a third group not yet in the position to use computers. My remarks are really relevant to the last two groups, since the first group usually has a good staffing ratio and is in the position to purchase expensive computer periphery equipment and to develop sophisticated systems. It is worth mentioning that the amount of effort put into setting up systems for intracavitary and interstitial radiotherapy is relatively small, compared with external beam work.

The comment might be made that this is all very well, but in the majority of cases computer output is by means of a line printer, and the radiotherapist is not helped in his decisions when he is confronted with large masses of numbers needing further interpretation, which takes up valuable time. This is basically a communications problem, it is where the dedicated systems mentioned in group 1 have made such a valuable advance. They provide a pictorial or graphic display that is recognized as the most efficient way to transfer large amounts of information. These displays can be rapidly and easily interpreted, and the operator can interact with the computer to change the display.

Technical development in the computing equipment field now makes available graphic display terminals that are expected to cost less than $5,000, approximately 50 percent more than alphanumeric terminals in 5 years time, which is a small fraction of the cost of the dedicated computer. These terminals can either be connected to a central computer over a fast telephone line, or linked to an in-house computer. The terminals I have in mind are in some cases a development of the alphanumeric display terminals, which I am sure many of you know about. The graphic terminal allows lines as well as alphanumeric characters to be drawn on the screen, and so builds up a picture of dose distribution.

The graphic display terminals are basically cathode ray tubes, and fall into two main groups:

(1) Storage tubes such as Tektronix 4002, where the picture is built up on the screen from information fed from the central computer. The picture remains on the screen for a long period of time. The principal drawbacks of this type of display are that if you wish to change any part of the picture, you have to destroy and start again; and that every bit of information has to come via the central computer.

(2) Random Scan Units, such as Cossor DIDS 406. These terminals contain a memory store used to display the picture on the screen. Changing the contents of the store changes the picture; and since each part of the store is addressable independently, parts of the picture can be changed without changing the rest. It is also possible to feed bits of information directly to this terminal, and so build up parts of the picture without connection to a central computer.

We have been repeatedly informed in the literature and by manufacturers on both sides of the Atlantic that a great demand for graphic terminals is expected in the next 2 or 3 years. Considering both alphanumeric and graphic terminals, it is anticipated that by 1980 the medical field could become the fourth largest user. The aspect holding up rapid development at present is the cost of developing software.

In the United Kingdom, we are fortunate that the Department of Trade and Industry has set up a group whose function is to give assistance to persons interested in Computer Aided Displays. The Middlesex Hospital has made a study of the use of low cost CRT display terminals, and estimated the cost of developing programs for a system that can be used for afterloading computer dosimetry. We have had to restrict ourselves to equipment either already on the British market, or likely to become available in the next year or so. The terminal we feel is most satisfactory for us is the Cossor DIDS 406, a member of the DIDS 400 series and a development of the alphanumeric terminals used in Data Select.

At present, I know of only one piece of equipment of U. S. manufacture comparable with the Cossor, and this is made by IMLAC - PDSI. With the price of small computers falling, one would not be surprised to see a number of small processors with CRT attached, and these would be presented at low-cost graphic terminals. In such cases the user would have to beware of software problems.

I now would like to suggest the jobs this kind of equipment can handle:

(1) Reconstruction of positions of radiation sources in implants and intracavitary insertions;

(2) Presentation of dose distributions in 2 or 3 dimensions, as required;

(3) Construction and dose calculations of proposed distributions that would be valuable for teaching and planning purposes.

The reconstruction and display of an implant should be able to be viewed in three dimensions, rotated, and viewed from any direction at the request of the operator. If this is done, the experienced radiotherapist can quickly know whether to accept an arrangement or make adjustments before afterloading. Presentation of dose distribution in two dimensions is commonplace, but in afterloading techniques one is dealing with a number of radiation sources deposited in a volume and lacking the symmetry of beam therapy. It is my personal view that there is need for three-dimensional dosimetry in afterloading.

Several methods of presenting three-dimensional displays will have to be tried. There will have to be some ingenious solutions, since the apparatus discussed here is not capable of the sophistication of the installations costing around $100,000, (for example the IBM 2250). The important point is that it is possible, but that the development of the software should not be underestimated. I would hope that within 2-3 years we will have systems that can be used over telephone lines. A large number of centers could use the graphic facilities. If the work done with dedicated small machines is anything to go by, I feel sure there will be a sizeable demand.

I now would like to back up my discussion with figures we have worked out, according to prices in the United Kingdom. I would like to emphasize that comparison and cost are based on ability to do a particular job. I fully recognize that if a department possesses its own small computer, it is able to carry out other jobs. But it also has the responsibility of running its machines in terms of maintenance and manpower, which every department may not wish to do.

The cost of typical treatment plans on 200 band timesharing systems in the United Kingdom is in the region of $10 to $12 per run. It involves using 6K store, 95 sec cpu time, and up to 20 minutes connect time to a large machine. This machine is an Atlas 2 computer, 131K, 48 bit words. If graphic displays are used, a faster telephone line will be needed, usually 1200 band. This could result in a reduction of connect time, and therefore a portion of the cost. For example, one would transmit the data to a central computer at one twentieth the cost of teletype, and 15 times the speed.

We considered the capital cost of setting up a remote graphics terminal compared with a small dedicated computer, and there is at least a factor of 6 in the costs. If one is to do three-dimensional displays, then a machine with at least 16K store is needed, and many people feel that one will end up with a 32K machine. In the comparison, allowance is made for capital depreciation, loss of interest on the capital sum, rental of telephone lines and modems, and servicing contracts. A pessimistic assumption is that using graphic terminals will double the computing charges for a teletype system, because of extra time spent with an interactive system. (This assumption is hotly disputed by C.A.D. specialists, who take the view that costs would be reduced by up to a third, because of the interactive nature of the system and higher data transmission rates.

If a 10-year life is allowed for the system (and this favors equipment of high capital cost), then TSS and dedicated machines cost much the same. If the expected life of the system is less than 10 years, then the costs favor timesharing.

There is, at this stage, room for considerable error in any estimate of this kind.

DISCUSSION

CHAIRMAN GLICKSMAN: A small number of questionnaires have been returned to us. Although this may not be a purely representative sample, we did get the following replies:

When asked about the advantages of computers to those people who now are using it, a large number -- about two-thirds -- said there is none in terms of time, but a great advantage in terms of accuracy. Cost certainly is no advantage. Innovative ideas were scored by practically all, with educational advantages sort of halfway in between. I wonder if members of the panel would like to comment, in terms of these responses.

MADAME DUTREIX: May I begin with some comment about the accuracy of computers. I think their accuracy may be as high as we want. It's possible to have an accuracy of 1 in 10,000 or more, if you wish. You can take into account anything -- bones, or tissue attenuation, whatever you will. But accuracy really is linked to the position during elapsed time. We take two radiographs just at one moment, we do not really know what happens before or after they were taken. This is a real problem.

MISS STOVALL: In 1966 Powers and some of his colleagues published a paper in which they compared four computer programs then in use. They compared quantitatively the output data, and found very good agreement. I think this sort of thing should be done with more programs now in use. We know too little about how the programs compare.

DR. NEWTON: Just a comment on the matter of cost. When one considers cost, one must look at what one is buying. If you wish to continue treating without the aid of complete planning that computers provide, indeed the cost would be less. But so presumably would be the benefits to the patient. When we speak of cost, we must realize that we're buying something more in quality of treatment, and be willing to pay the price for it. The difficulty is that it's virtually impossible to devise controlled clinical trials to demonstrate that benefit. I guess it's really an article of a faith that better treatment planning will pay off in better results.

I am interested, though, in Shalek and Stovall's earlier paper showing that retrospective examination in a number of implant cases of oral carcinoma where there had been treatment failures, due either to cold spots or necrosis, revealed that in 80 percent of the cases the computer would have identified inadequate treatment planning.

MISS STOVALL: Yes, we found that in 80 percent of the cases where there were complications these could be explained on the basis of poor dosimetry or poor geometry of the sources. However, something we did not make clear is that we looked at a number of cases that did not have complications, and the very large majority of these did have good dosimetry. There were a few flukes that should have had complications, but did not. I think this is the sort of thing you would expect to find clinically.

MR. JAMESON: I think computers provide not only accuracy, but consistency of standards. When you're using a computer program you're given consistent accuracy, and it provides you with a basis for comparison at a later date.

MR. HOLT: I'd just also like to comment on the use of computers. The Memorial time-sharing network originated in 1967, and it started with four collaborating institutions. By now it has built up to well over three dozen collaborating institutions. I think this number certainly will be doubled by next year. These people spend as much as a thousand dollars a month on the system. Perhaps some of these costs are chargeable to patients, we have no way of knowing. But feedback from the users is that they have found it sufficiently useful to spend that kind of money.

MR. SILER: As far as cost is concerned, we have our own computer which is quite fast, but about two blocks from the radiation therapy center. For this and other reasons, we chose to utilize the Memorial time-sharing system. We started out with costs of about $300 a month, now are running close to $2,000. What's happening is that the system not only is gaining acceptance, but increased usage. The residents come in at night, punch in their little key, and play with it. It's now getting to the point where we can't support the cost. What are we going to do?

I think that in this case we're going to have to look to Dr. Newton. We are getting to the point where, with demands upon time-sharing by the sophisticated user, the system is beginning to be inadequate. The time-sharing system is beautiful, I certainly recommend it very strongly to people who are not using anything.

DR. PIERQUIN: I have just a modest remark from the clinical point of view. I think we must see a difference in simple implants that can be controlled by manual dosimetry without important error.

But there are other locations where the use of a computer is quite necessary; for example, in cervix cancer.

DR. SUNTHARALINGAM: I would like to pose a question regarding the accuracy of dose computation. One point seems to have been missed: accuracy depends on accurate specifications of the activity of the radionuclide. How has one determined the accuracy of the activity of these individual sources? Also, how does one do the dosimetry for iridium 192 when in the open literature there is up to 25 percent variation in the published specific gamma-ray constant for iridium?

MADAME DUTREIX: Accuracy in the specified activity of iridium wires certainly is as good as the specified activity of radium. When you buy radium sources, activity is given plus or minus 10 percent. I think we are able to measure the activity of iridium with equal accuracy. As far as gamma constant is concerned, I think it's not so important. The activity of iridium wires is an apparent activity, so I think that is just a play on words.

DR. SUNTHARALINGAM: What I actually have in mind is that the National Bureau of Standards in this country calibrates radium sources. One is able to compare their true activity, even if bought from different manufacturers. I will give you an example regarding iridium.

For the past 1-1/2 years we have been purchasing iridium from Paris. We have come up with an assay system of our own. Our discrepancies initially ran 20 percent from the activity specified by the manufacturer. On communicating with the manufacturer, to my surprise I got a reply saying there was an error in their ionization chamber measurement, and the factor changed another 10 percent.

Since the discrepancies exist, I now pose these questions to clinicians and physicists. To the clinician: How would you like the source strength of radium substitutes to be specified? And to the physicists, especially those working in national laboratories: Could you come up with a system whereby one can accurately measure the activity of radium substitutes?

MADAME DUTREIX: I realize there is a problem. When you buy iridium wire, you have to specify if you want calibrated or just ordinary wires. If you don't ask for calibrated wire, you get just a rough value and it is your responsibility to measure the exact activity. This is a problem, but not a very difficult one. You can have one calibrated source as a reference source with which you just compare the activity of the other sources.

The real problem is to be sure that activity is not too different from one wire to another, so that you can assume the same activity in several wires used at the same time. Also you have to be sure that you don't mix wires of one age with those of another; you must be able to check quickly the activity of a source.

This is a real problem which must be solved in your own laboratory. If the laboratory is not able to check the activity of wires, it's very dangerous to use nuclides. But I am afraid it's also dangerous to use radium.

DR. HENSCHKE: I would like to pose a question and challenge to this panel of eminent physicists. We have those beautiful computers and isodose curves, but for us clinicians that's really only one part of the problem. Because we don't know where the tumor is. Isodose curves might have the most beautiful and even distribution, but we may be treating normal tissue.

I think something should be worked out to specify in drawings where the tumor is. Until we have that, computer dosimetry is not as useful as it could be because we never can actually relate it to tumor. In interstitial therapy, of course, the tumor is very small, and a slight malposition will be of great consequence.

Another problem concerns uterine cancer dosimetry with cervix applicators. For the past 3 months we have been running cancer therapy in Jamaica. Every day we have two or three cervix applications. The tragic thing in the countries where you have a lot of cervix cancer is that you just don't have the means for time-sharing. Those of us in richer nations really owe the other countries some measure of consideration. I would like to suggest some cervical system that could be used with a very simple computer for isodose curves.

DR. ROSWIT: We apply these exquisitely accurate values from the computer to a crude anatomical drawing by a resident who isn't a Michelangelo, and pretend we're doing the right thing. This has been going on for a long time. Most of us use anatomical atlases drawn from a frozen cadaver; sometimes those by Dr. Simington of an Irishman who died in Dublin in 1936. We still use this today.

It seems to me the most realistic model is the patient himself with all his problems, his anatomical variations, and the variations produced by the tumor itself. And this pattern can only be acquired through transverse tomograms. In the radiation center of the VA Hospital in the Bronx, we have been using transverse tomography since 1956. I don't think I'd get half a dozen hands here today of individuals who are using the helpful transverse tomograph.

PROF. A. HOCHMAN (Jerusalem): We radiotherapists are trained from the beginning to be very accurate. The question is how much accuracy is relevant to our success or failure in the treatment of cancer. In other specialities, physicians will not hesitate to say they are accurate, though citing doses varying as much as a million and a half units of penicillin.

I saw here a tumor shown by Prof. Chassagne, a huge squamous cell carcinoma in which there were viable and necrotic parts, oxygenated and unoxygenated cells. There were variations even in the histological components of the tumor. Some parts may have been well-differentiated, some were anaplastic. In all these variations in the tumor, we apply a uniform dose. I think it would be biologically relevant if we could really give more treatment to the hypoxic regions, less treatment to the differentiated, and even less to the anaplastic. But we continue to use a uniform dose.

So I'm joining the two heretics who were talking about extreme accuracy. The question is, how much accuracy do we need in treating a cancer patient, when biological variation in the tumor itself probably is the greatest cause of our failures in treatment? Not the skill, not the accuracy, but the biology of the tumor. Seeing extreme concern for accuracy, I sometimes am reminded of trying to measure a mile by using a unit of an inch.

DR. NEWTON: I agree that anything we do here is rendered imperfect by lack of detailed knowledge of our target. Transverse tomography gives you a chance to individualize where you think the tumor is. Extent along lymphatics and vasculature is something we cannot ever see.

The problem about oxygenation is important. I suspect you are acquainted with Dr. Fisher's work; if not, I'd like to recommend it. He is trying to develop treatment strategy in the timing of exposures that will take advantage of oxygen enhancement ratios and recovery. I'm doing a little work in this area, too. The information one needs here is based on cellular kinetics, and I think it's going to be a long time before we can do a proper treatment of the cellular substructure of the tumor.

What are we going to do meanwhile? Let's concede that our knowledge of the structure of the tumor is imperfect. I think we should just do the best we can. The computer is not to be looked at as a device that gives you the entire answer. The issue is accuracy and precision, but an answer to six or eight places is not important. It is important to place dose distribution where the therapist thinks it should best be placed on the basis of knowledge, tomograms, or whatever you can bring to bear on the situation. Accuracy beyond two or three places probably isn't going to get you much farther, anyway.

MR. SILER: The comments by the gentleman from the floor are appropriate, but they also are dangerous. There is legitimate criticism that the physicist is trying to be overly precise, in relation to the current lack of clinical and biological information; that computering is used as an excuse for just being sloppy, and not making use of techniques that are well-known and established in virtually every major medical center.

Time-sharing still is not being used in the smaller hospitals. So it's partly a question of trying to educate physicians to find out where their dose is going, and how much is going there. It's long past time in the major centers to quit worrying about what system you're going to use to calculate dose distribution. We should divert our attention to the questions of tumor localization.

Transverse tomograms are helpful. Even when you use an old cross sectional anatomy slide from some poor guy who got frozen and sliced up 20 years ago, you're beginning to get someplace. But of course this still is not enough.

Perhaps we should turn our attention to the improvement of diagnostic radiology. Some of the techniques that have been developed in jet propulsion laboratories for the enhancement of film images have not been really applied. Nobody knows what we can't do with the diagnostic film to help improve chest x rays, or a scan. There is work to be done here; maybe we ought to quit patting ourselves on the back for our nice treatment plans, and get to work on some of the real problems.

DR. ROSWIT: If you're going to encourage people to continue using that cross sectional atlas, your computer is going to give you the wrong answer with the highest degree of accuracy.

DR. PIERQUIN: I think there are two points in response. The first is a biological problem. We think that by continuous irradiation with low dose rate, the difference in response between oxygenated and nonoxygenated cells is rather insignificant. For the same dose there is nearly the same effect. There may be a more significant difference in fractionated irradiation at a high dose rate. There is, perhaps, an advantage for low dose rate in interstitial radiation.

The second is a dosimetric problem. I think that progress in the techniques for accurate dosimetry is very important in the cure rate of tumors treated interstitially. I can give you an example from a comparative study we made of an empirical system with radium about 20 years ago at Gustav-Roussy for cancer of the tongue. We compared the results of the early cases with 200 more recent cases treated with the help of transverse tomograms and computer program for accurate dosimetry. The results in the more recent cases were far better.

DR. CHASSAGNE: As a physician, I want to comment on the use of computers in cervix cancer. We formerly treated more than 250 cases with calculated doses, and now don't know exactly what doses we used. We improved our technique with computer calculation, now get better results much fewer complications. We avoid practically any complications in the bladder, and that is important. It's true that we don't know exactly where the tumor is, and that we should make progress in how to localize it in the rectum, how to localize it in the bladder, how to localize it in the sigmoid. We are trying to improve our localization techniques; but this requires much more work.

DR. HILARIS: It seems that the floor is taken by the clinicians so I am tempted to take just 2 minutes. Right now I think we couldn't work without a computer at Memorial. If you take the example of uterine applicators, perhaps you don't need a computer in individual applications. You probably can work with milligram hours if you know the distributions of the sources, the distance between the vaginal ovoids, and so forth. But when it comes to combining the doses from various applicators, if you're going to know exactly what you're giving to the rectum or the bladder, as Dr. Chassagne mentioned, you'll find the computer invaluable. It is even more important in interstitial therapy.

Just one minute about defining the tumor volume. I was hoping that Mr. Holt would comment on that. We have used two ways to outline the tumor. The first is to reconstruct the implant with dental compound, and make a positive model of the implanted tissue. This is very useful in superficial removable implants, the physicist can work out the dose distribution with three-dimensional visualization. A second way is to mark the peripheral seeds in the implanted volume in a set of orthogonal x ray films. The isodose curve which encircles at least 95 percent of all seeds indicates the minimum tumor dose. This was found to be very useful for permanent implants.

But more important for permanent implants, we found that we could not use the Paterson-Parker or Quimby tables with the iodine seeds of low energy that we have been utilizing recently. The computer can give us the complete dose distribution. It appears that small variations in the dose are not very important. In general, this applies also to radium or gold seeds. But that depends on the volume.

It is not significant if a small portion of the tissue receives even 100 percent higher dose if the volume is very small, only 1 or 2 cubic centimeters. It becomes significant if a large portion of the tumor gets a high dose. Right now the Physics Department at Memorial is able to give us the dose versus volume data, as I see Dr. Newton can do.

DR. LIEGNER (St. Luke's Hospital): I've been fortunate in being able to participate in the Memorial Hospital program as a satellite, and I think we also contribute somewhat in the feedback. From the point of view of our institution, we also feel strongly we could not get along in radium work without the computer. The cost in our institution is born by the patient, or perhaps the insurance company; the hospital has accepted a charge of $40 per treatment plan. The input is done by our physicist and technologist on the basis of orthogonal films.

I'd like to present to the panel the possibility of altering the plotter output before we get the wonderful display system that Dr. Newton has shown, a demonstration on the screen of what a poor man's plotter is. We take the output on a teletype, and on each of the planes we select draw isodoses either in dose rate or in kilorads. Then we take simple, thin plastic sheets and lay one upon another to build up the model. Each isodose is in a different color, specifying the doses around the source.

I would like the panelists to suggest or perhaps think about ways in which the output could come out on clear sheets of plastic which we then could build up into a three-dimensional model. In this model we have the mockup of the sources in the appropriate plane, we have the bladder and the rectum opacified.

MR. HOLT: May I answer Dr. Leigner's question, which is of general interest. I did show a plotter in one of my slides, and we are presently working to adapt it. That may take some time. But we have all the information, except the plotting routine. At the moment we're writing it for a plotter available on the general market, I think, for $1,800. I don't know whether it will work on a clear sheet of plastic, but you'd be able to do isodoses on different sheets of paper with it.

DR. NEWTON: I think that probably would be the best immediate way to go. But you really don't need to have your information to scale. If you could take it in your hand and look at it from different directions, I suspect that would do just as much for you as if you had it in true scale and looked at it that way.

I don't know how they do this, but Bob Ledle and Margaret Dahooff in Washington have used a photographic technique where they draw the output from programs on x ray refraction and molecules on lantern slides. Then they take the transparent slides and stack them on top of each other, much the way you've done with your celluloids. Thus they are able to view it from different angles.

But one thing you did mention is very, very important. That's the question of color. For many years now we've called on industry for cheap graphic scopes. We've shown that we will use them if they are provided. Now that we've created the demand, I think they are going to get cheaper.

Now I think we've got to start another campaign. Those of us in medicine who have to make judgments on complex, three-dimensional data, anatomical structure, dose distribution, source locations, etc., have just about run out of what black and white representations will do for us. I'd like to encourage more statements of the need for color, because I believe that we eventually should have graphic terminals or celluloid representations in different colors for the isodose plots, the organ systems, and the applicators. This is not just to make it more pleasant; it's to make it readable, because it gets very, very complex in black and white. Many of the things I bring up on the scope are so complex that I wonder if they're doing me all that much good.

MR. PARKER (Richland, Washington): May I begin with an admonition before I ask a question? This is a conference sponsored by the Public Health Service, and in the far corner of the room sits one of our country's experts on the hazards of color television. By the time these new computer systems get to color, which would be desirable, I hope greater attention will be paid to potential hazards from that source. I'm sure Arve Dahl will be glad to help you with any questions on that. End of admonition.

Now I'd like to go back to an earlier question on the activity of sources, and suggest that uniformity of distribution along the length of the source possibly is more important than activity. As early as about 1937, I believe, Griffith demonstrated radium needles in his laboratory that had something like 20 percent more activity in one half of the supposed active length than in the other. With sources like that, neither hand calculation nor computer calculation can give you the right answer.

I think the modern sources, iridium and so on, are much better. Perhaps the panel has some direct measurements on the uniformity along the length of today's sources.

MADAME DUTREIX: You are right. We checked our iridium wires for uniformity of activity. We measured the activity of only one centimeter, shielding the rest of the wire. The homogeneity of activity along the wire was very poor. Now it's much better, but we still check every wire.

MR. DERACAL: I have a question about the programing of computers. For example, the Memorial program has the radium needle as a point source. When you put it into an implant, there seem to be cold spots in the computer printout; whereas if you take 3 points along different points in the source, you'll find no cold spots. I'd like to know if they have any computer programs that actually show the source as a finite length rather than a point source itself?

MR. HOLT: Actually the Midas program consists of three parts. One is the point source program that you mentioned. In addition to this, we have a table that calls on the experimental depth dose curves used for iodine 125. More recently, we have programmed the Sievert integral for radium sources. Unfortunately, this does not help you with iridium needles or wires. At the moment, we have not utilized the Sievert integral for iridium, since the attenuation would be different.

MISS STOVALL: Our program uses the Sievert integral for linear source calculations. I might add that another program to calculate tables of dose rates from linear sources uses a slightly different approach. We worked a source into a number of point sources, and we found that for sources 3 centimeters in length you have to break each into as many as 40 point sources in order to get the same accuracy as Sievert integrals. This gets within one-half percent the same dose rate as the Sievert integral, at points 2 or 3 mm from the source.

Mme. Dutreix has mentioned combining teletherapy dose distribution and brachytherapy, and I would be interested in comments from anyone who is doing this sort of combining of dose rates. How do you cope with the problems that have been mentioned?

MR. HOLT: Accurate calculation of a combination of internal and external beam is very difficult because it is a three-dimensional calculation. We have made several attempts to describe a combined dose distribution; in fact, we have made several attempts to design special blocks to complement internal dose distribution in places where we wanted to use external beam radiation. But we're not using this on a routine basis, at present.

We are, however, matching isodose curves and looking at isodose curves in one plane. This is a different problem, its complexities are not nearly as great as trying to look at the three-dimensional distribution. But I think if one has isodose curves in a plane, and restricts the external applications of a beam to relatively simple techniques, one can form a composite isodose curve that will establish the upper and lower limits of irradiation in the general area of interest. In the pelvic nodes, one can get a very accurate idea of the dose distribution.

MR. JAMESON: I think this problem really is a twofold one. If, for your purposes, you merely want to know how to add the two types of radiation -- interstitial and external beam, for instance -- we currently do it at present in rads. In this case the radiotherapist knows what dose he wishes to give in both cases, even if he knows it only by empirical standards.

If, however, you wish to take account of the equivalence of low dose-rate continuous irradiation and high dose-rate fractionated irradiation, then this is a completely different problem. It's a research topic.

MADAME DUTREIX: Forgetting for a few minutes the problem of rads for continuous and fractionated irradiation, we still have two problems to solve. The first is related to cervix cancer. The position of the cervix is never the same during irradiation by iridium or radium and by external radiation, because of the problem of maintaining the source in the patient.

This is a very difficult problem. You have to assume that you add rads near the cervix or with reference to the bones, for instance. If you want to take as reference points the bones of the patient, there is a new problem. Very often there is rotation of the pelvis between the two irradiation, due to the presence of radium or iridium. The position of the patient is not the same as when she's just lying on the table without any foreign bodies in the cervix and vagina.

So we have a program, we can add rads in any plane chosen by the radiotherapist. However, we never use it routinely because we do not know how to solve the problem of the variation in anatomical relationships.

MR. SILER: This is one place where afterloading techniques offer a tremendous advantage, if you can leave in place the device into which the radioactive material is loaded. We worked very hard and devised a pretty little wedge designed to marry beautifully external radiation to a tandem. It's completely useless, because if you make an error of half a centimeter you get a tremendous hot spot on one side and a big cold spot on the other. If you are going to try to marry these distributions in the region of the tumor, you'd better have something there to tell you where the irradiation actually was, like dead seeds.

This perhaps can be quite easily handled by computer. It requires work by the physicist and therapist, so they can confidently state that they are not just adding numbers that have no reference to what the patient actually got.

MISS SNELLING: I don't know how much impact Dr. Frank Ellis has had on this side of the Atlantic, but at home any discussion concerning the addition of treatments of different energies, especially at different dose rates and at rates that change throughout treatment, would always be associated with some thought of his ideas on the nominal single dose. This concept, of course, is something that only a computer can add into our programs.

DR. CASTRO (New England Medical Center): I have two questions, really. The first is with regard to the fidelity of the isodose curves. Are there any facilities for dealing with the problem of missing points, points we know we should measure but can't because it's not obvious where they are on the films?

The second question: Since in the near future somebody is bound to question whether what we have done is worthwhile, isn't it about time we used computers to establish some kind of a patient data bank? We have something like that at the New England Medical Center, but so far we are the only ones using this bank. If anyone is interested, we would gladly supply more information.

MR. SILER: K. C. Tien, who started this whole thing going, is now working part time at Downstate Medical Center precisely on the problem of a meaningful data bank.

MR. HOLT: The problem, if I understand it correctly, is to localize seeds and in orthoginal radiographs, particularly in obese patients where the seeds may not show up in the lateral. This can be solved by computer if it also is possible to take stereo shift films. We now have a method that is still in the experimental stage. It eliminates the problem of positive identification of the seeds on the radiographs by the person digitizing the radiographs, derives its information for analysis from a set of stereo as well as orthogonal radiographs.

DOSIMETRY

ASPECTS OF THE DEVELOPMENT OF IMPLANT DOSIMETRY

John S. Laughlin, Ph.D.

My report is concerned with developments in implant dosimetry since World War II. These developments have dramatically and drastically affected all implant dosimetry. They are directly related to changes during the same period in external radiation therapy, that preceded and instigated much of current implant dosimetry.

Other radiologists and physicists have commented on the significance of developments in radiology that encouraged the growth of radiation therapy as a full-time profession and separate discipline. Last year, at the annual Failla Lecture before the Radiation Research Society meeting in Dallas, Dr. Henry Kaplan called attention to some of these changes (1). His address was primarily a review of developments in radiobiology, and in it he pointed out the future directions of research that are necessary if radiobiology is to make a significant contribution to radiotherapy. He commented that although studies in radiation biology have contributed not one example of significant improvement in the cure rate of human cancer to date, substantial gains have been contributed by physicists by the introduction of megavoltage apparatus and improved dosimetry.

Until well past the end of World War II, most external therapy in this country was carried out by apparatus of 1,000 kv or lower, primarily in the less than 300 kv range, and generally on a part-time basis by diagnostic radiologists and some surgeons. Due largely to the initial efforts of Professor Kerst and Dr. Henry Quastler (2), the potential advantages of high-energy x-rays and electrons were outlined. In the years immediately following the War, betatron x-ray and electron beams (3) were developed and clinically applied, followed quickly by telecobalt gamma-ray beams and linear accelerator high-energy x-ray and electron beams. These developments with associated changes in dosimetry and treatment planning procedures have had an impact on cure rates achievable by radiation as well as on the discipline of radiation therapy.

With the realization that radiation energy can now be localized within the patient to a far greater extent than previously was possible, it became worthwhile to concentrate greater effort in the development of treatment planning procedures and of lesion localization technology. Description of the distribution of radiation dose, either in two dimensions throughout a given plane or in three dimensions, are necessary to exploit adequately the advantages of these high-energy radiations. In order to facilitate radiation dose distributions on a regular basis for the treatment of large numbers of patients, a great many computations are required, and the development of analytic expressions (4) as well as the use of automatic computation methods were considered.

In 1954 the Director of the Memorial Sloan-Kettering Cancer Center authorized the rental of IBM card sorting and handling apparatus explicitly for radiation treatment planning trials (5). Our staff first applied this approach to telecobalt rotation (6). For resident instruction, we still employed the very useful method developed by Carl Braestrup (7). At the same time, this automatic approach was also applied to internally administered radioactive isotopes. If it is important to know the distribution of dose in a patient when radiation is applied externally, it is just as important to know the distribution when radiation is applied internally. Correlation of biological response with dose required this knowledge. There was the additional motivation that in many cases both external and internal radiation sources are employed on the same patient, and it obviously is necessary to know both dose distribution with equal certainty.

The first publication on computerized implant dosimetry, "The Application of Automatic Computation Methods to Implant Dosimetry," was presented at the annual meeting of the RSNA in 1957, and appeared in Radiology in 1958 (8). This initial achievement of computerized implant dosimetry was the work of Richard Nelson and Mary Lou Meurk, both them now active hospital physicists with their own groups.

This development has continued at our institution, where the various implant programs and associated procedures are incorporated under the term MIDAS ("Memorial Implant Dosimetry Automated System") whose development is described in the literature (9, 10). Other systems have been developed in other institutions (11-13); and much of this development has been carried out and reviewed by Shalek and Stovall (14).

One procedure in our MIDAS system that we have found particularly valuable is the use of a digitizer in conjunction with analysis of the coordinates of a source on the radiograph. The digitizer makes it convenient to record on punch paper tape the two-dimensional coordinates of any point revealed on the radiograph. In this way, the coordinates of seeds as they appear on any projection can be conveniently transferred to the computer. Equipped with two-dimensional information from stereo pairs, the computer can determine the three-dimensional coordinates of the seeds, which then are applied in the MIDAS program to produce dose distribution in any desired plane. Since the planes can be rotated, a three-dimensional presentation is possible with any degree of resolution the clinician desires.

It has been the experience of our group that computerized dosimetry is necessary for all internal uses of encapsulated radionuclides. Although atlases can be helpful, we consider them useful for planning purposes only. Not only is the custom computation much more satisfactory, but it can be achieved in less time than modification of atlas distribution. This applies to all encapsulated radionuclides, with possible exception of the Ernst applicator with sources fixed both in activity and geometry. Whenever one uses an applicator in which source activity can vary, custom computer analysis is recommended.

To illustrate routine procedures for implant dosimetry, I shall use four recent applications different radionuclides: cobalt 60, iridium 192, radium 226, and iodine 125.

The first case involves the use of a cobalt 60 oscillating source in a removable applicator. This particular application was in the nasopharynx (figure 1). The sources were positioned in 5 locations, each 2 mm apart, and computations were carried out on that basis. As can be inferred from the reviews routinely prepared in such cases (figures 1, 2), both demagnification and dose computation are carried out automatically, together with a three-dimensional computation of the volume of tissue receiving any specified dose level.

The second case shown is a removable iridium 192 implant. This was an anaplastic epidermoid carcinoma, and external radiation therapy was applied through opposing fields including the nasopharynx and entire right neck. The highest dose in the lesion was 4,600 rads, delivered in 5 weeks. At the end of treatment the nasopharangeal mass had disappeared, and the right cervical mass decreased in size. The iridium implant consisted of 6 ribbons arranged in 2 planes: 4 of them in the deep and 2 in the superficial plane. Four of the ribbons contained 9 seeds each, the 2 remaining ribbons contained 6 seeds each, a total of 48 seeds (figures 3, 4). The radiographs were obtained with dummy sources strung in the inner nylon tube inside the larger nylon ribbon. The digitizer was employed, as in all cases, to obtain the coordinates of the dummy sources from the radiographs, since the active sources would be inserted in the same fashion. The implant delivered an average dose of 4,000 rads to the residual tumor. The lateral projection in figure 4 indicates the seed locations in the ribbons, as well as the reasonably uniform dose distribution produced throughout residual mass.

The third case involved epidermoid carcinoma of the cervix treated with a removable radium insertion. External irradiation previously had been delivered with cobalt 60 gamma rays in a midline dose of 4,000 rads. The Henschke applicator was employed, permitting differential loading. Two of the sources were 25 mg, three were 12.5 mg, one was 5 mg. Each of the radium tubes was represented by the two point sources for the dosimetry analysis. The digitizer was employed with the radiographs for analysis of the 3-dimensional location of the sources. The curved geometry of the applicator makes projection somewhat difficult. Figures 5 and 6 illustrate the location of the applicator and the distribution of radiation dose in each of the two projections.

The last case involves permanent implantation of 23.5 mCi of iodine 125 in a residual mass in the mediastinum resulting from Hodgkin's disease. Previous treatment by linear accelerator x-rays raised the dose in the mass to 5,000 rads. Chemotherapy had no effect, and since the mass was inoperable, iodine 125 implantation was carried out. The digitizer was used to analyze the anterior and lateral radiographs to determine the source coordinates. Of the 47 seeds implanted, 45 were located and 3-dimensional coordinates for each established. Figures 7-9 show part of the routine dosimetry report on this permanent implant. They indicate not only the geometrical location of the seeds with regard to anatomy, but also the actual dose distribution. The minimum total dose as a function of volume is also computed.

The symbols are identified in figure 9 all the information being printed by the computer. Dose distributions in two planes were requested by the clinician; it should be emphasized that the MIDAS program makes it possible to provide the dose distribution in any desired plane with any angular relation desired. In all 4 of the above cases, external radiation had been employed previously; the dose distributions were known and could be taken into consideration in planning the additional radiation to be administered by local insertion.

The same MIDAS system is also employed to compute internal isotope dose distributions for associated hospitals by means of our teletype system. As programs are developed and worked out in the MIDAS system, they eventually are made available to the external dose distribution computation service.

Of all the components needed in a hospital for computerized implant dosimetry (or external radiation dosimetry), the computer is the least necessary item. It is primarily the direction of the radiological physicist and programming skill that are indispensable.

The writing of programs and their continual updating to accommodate different situations, shapes of wedges, field shapes, and energies all require a great investment in skill and time. Accordingly, when requested by other hospitals to carry out treatment plan computations, we have always done so. This was carried out for several years by mail or personal courier. However, the possibility of using teletype and facsimile machines was investigated, and the details for more convenient transmission of treatment plans were worked out under the direction of Garrett Holt and Stephen Balter.

As a result, in March 1967 it was possible to inaugurate the Memorial Dose Distribution Computation Service by teletype with St. Luke's Hospital in New York City, and the Mt. Zion Tumor Institute in San Francisco (15). Other hospitals were added within a few months. Indicated in figure 10 is the distribution of 30 of the 37 hospitals now serviced on a regular basis by this system. It is interesting to note that although most institutions have a far larger number of external than internal cases, the ratio of plans for which they request computation is almost 1 (implant) to 2 (external).

In conclusion, I should like to emphasize that implant dosimetry is on the same firm basis as external radiation dose computation. As radiation therapy increasingly demonstrates its ability to improve cure rates, and is accepted as an alternative or necessary adjunct to surgery or chemotherapy, these dosimetry techniques should continue to help achieve this improvement.

(The author wishes to acknowledge the assistance of Stephen Balter with the cases chosen for illustration. The cooperation of Dr. S. Hopfan and Dr. B. Hilaris, for whose patients the dosimetry analyses were carried out, is also gratefully acknowledged.)

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 DISPLAY CASE NASOPHARYNX APPLICATION  AFTERLOADING   CO-60
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                                    :-----------------------------:
                                    :     SYMBOL  :       RADS    :
                                    :             :  FROM  :  TO  :
                                    :-----------------------------:
PROJECTION - LEFT LATERAL           :       F     :   500  :   707 :
MAGNIFICATION OF Z=1.34             :       1     :  1000  :  1414 :
MAGNIFICATION OF Y=1.32             :       2     :  2000  :  2828 :
                                    :       4     :  4000  :  5656 :
                                    :       6     :  8000  : 11313 :
                                    :       8     : 16000  : 22627 :
                                    :       *     : 32000. & MAXIMUM:
              TRACE OUTER DIGIT FOR ISODOSE CURVE
```

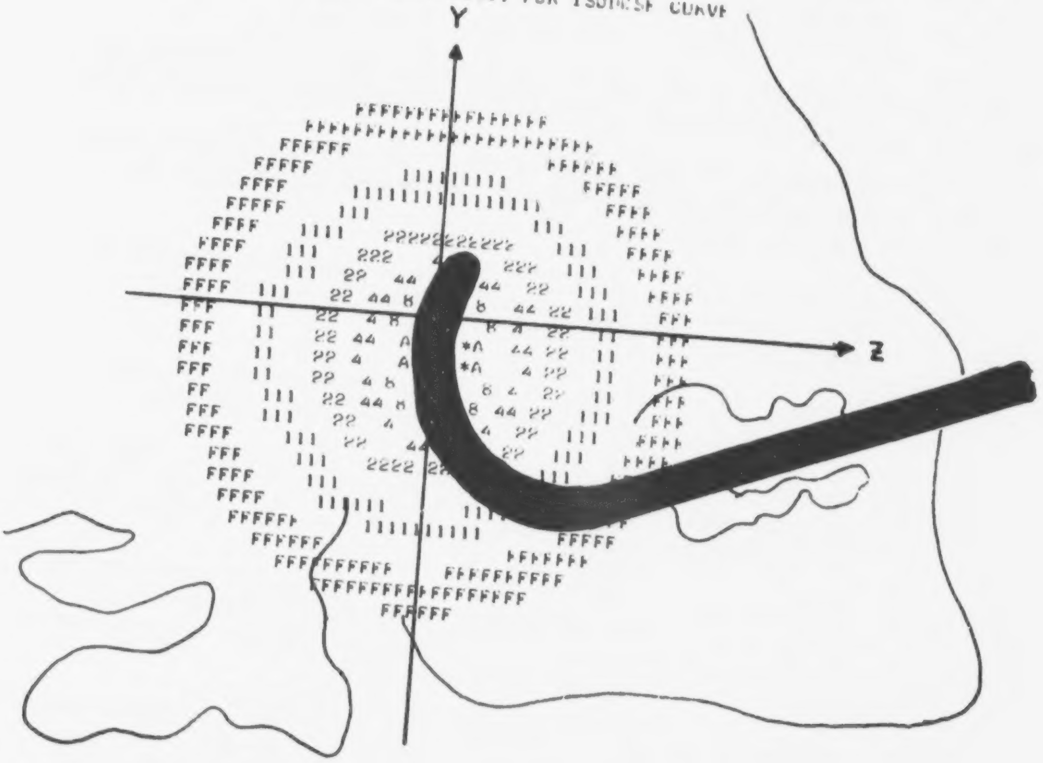


Figure 1. Automatic computation of dose distribution in lateral plane for an oscillating cobalt 60 source in a removable applicator in nasopharynx.

```
DISPLAY CASE   NAS0PHARYNX APPLICATI0N  AFTERL0ADING   C0-60

INVERSE SQUARE CALCULATI0N       :           SCALE                :
                                 :--------------------------------:
Z= 0.0                           :   SYMB0L   :       RADS        :
                                 :            :  FR0M  *   T0     :
                                 :------------:-------------------:
                                 :     F      :  500   :   707    :
PR0JECTI0N-A.P.                  :     1      :  1000  :   1414   :
MAGNIFICATI0N 0F X=1.39          :     2      :  2000  :   2828   :
MAGNIFICATI0N 0F Y=1.30          :     4      :  4000  :   5656   :
                                 :     8      :  8000  :   11313  :
                                 :     A      :  16000 :   22627  :
                                 :     *      :  32000 : MAXIMUM  :

              TRACE 0UTER DIGIT F0R IS0D0SE CURVE
```

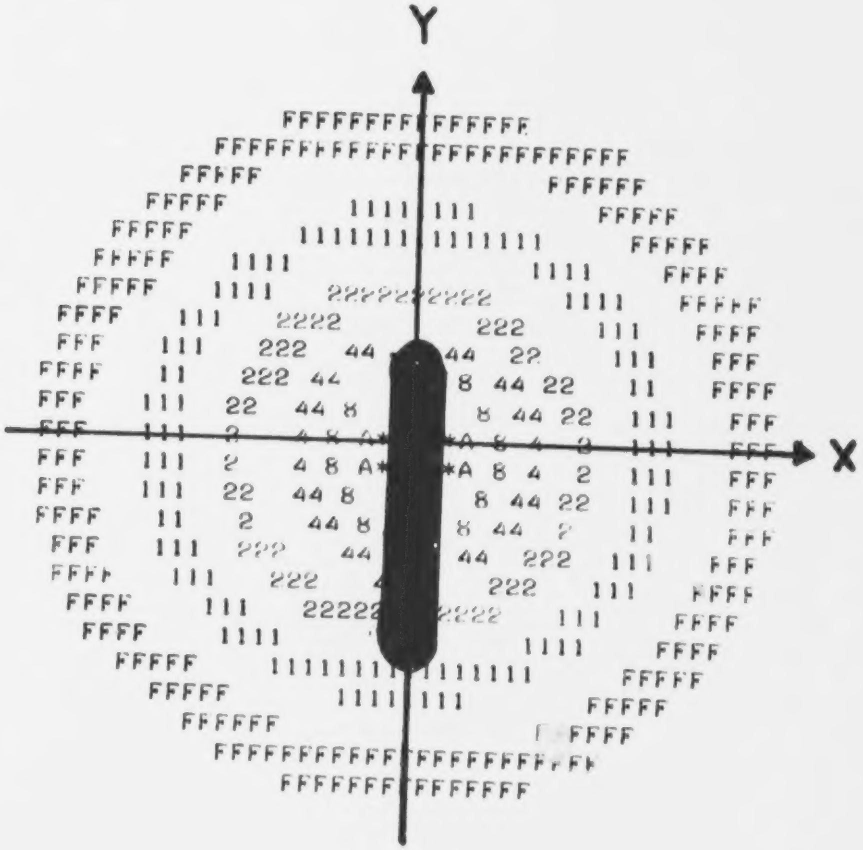


Figure 2. Computed dose distribution in plane normal to applicator for oscillating cobalt 60 source in figure 1.

```
DISPLAY CASE  IR-192  AFTERLOADING

INVERSE SQUARE CALCULATION    :              SCALE              :
                              :---------------------------------:
Z = 0.25                      :    SYMBØL    :       RADS       :
                              :              :  FRØM  :   TØ    :
                              :--------------:--------:---------:
PRØJECTIØN - - P.A.           :      F       :  500   :   707   :
                              :      1       :: 1000  :  1414   :
                              :      2       :  2000  :  2828   :
MAGNIFICATIØN = 1.35          :      4       :  4000  :  5656   :
                              :      8       :  8000  :  11313  :
                              :      ^       :  16000 :  22627  :
                              :      *M      :  32000 : MAXIMUM:

             TRACE OUTER DIGIT FOR ISODOSE CURVE
```

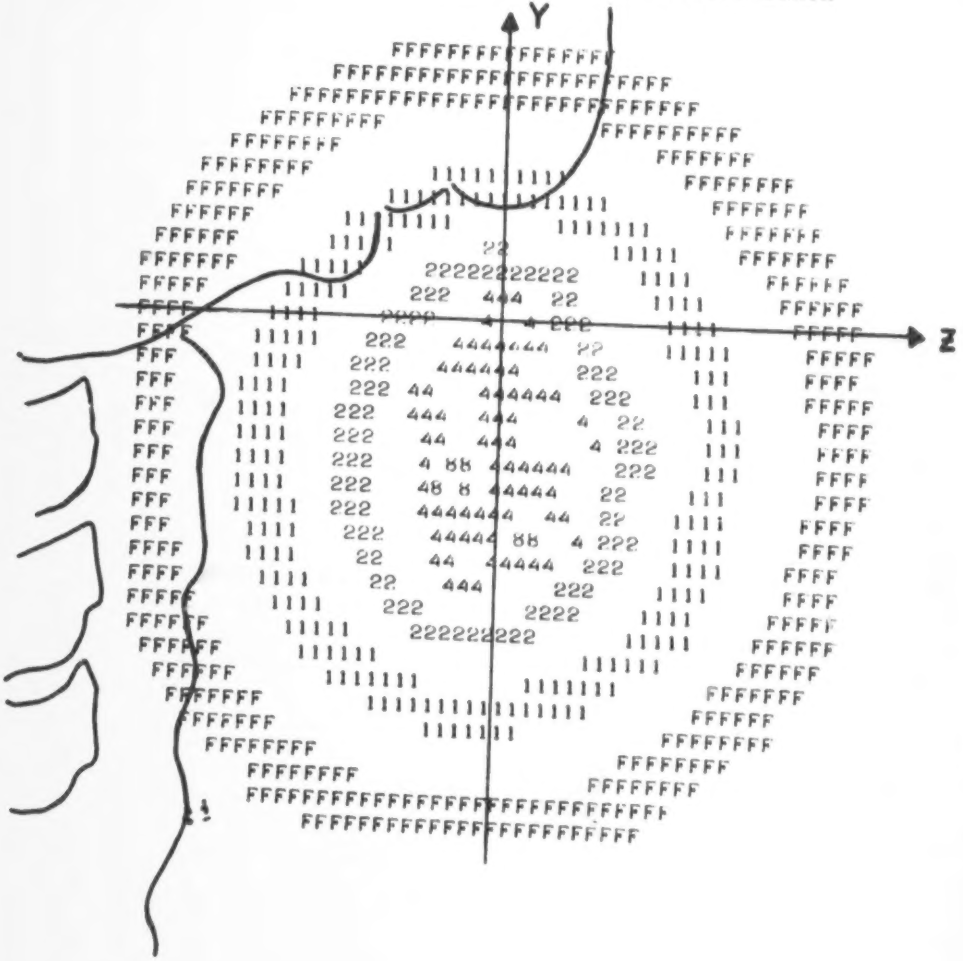


Figure 3. Removable iridium 192 afterloading implant for epidermoid carcinoma in nasopharynx and right neck. Dose computation shown in plane normal to 6 ribbons containing 48 seeds.

```
DISPLAY CASE  IR-192  AFTERLØADING

INVERSE SQUARE CALCULATIØN       :                 SCALE                 :
                                 :---------------------------------------:
Z =-0.19                         :     SYMBØL    :         RADS          :
                                 :               :   FRØM    :    TØ     :
                                 :---------------:-----------:-----------:
PRØJECTIØN -- LEFT LATERAL       :       F       :    500    :    707    :
                                 :       1       :    1000   :    1414   :
                                 :       2       :    2000   :    2828   :
MAGNIFICATIØN = 1.54             :       4       :    4000   :    5656   :
                                 :       8       :    8000   :    11313   :
                                 :       A       :    16000  :    22627  :
                                 :       *       :    32000  :  MAXIMUM  :

                TRACE ØUTER DIGIT FØR ISØDØSE CURVE
```

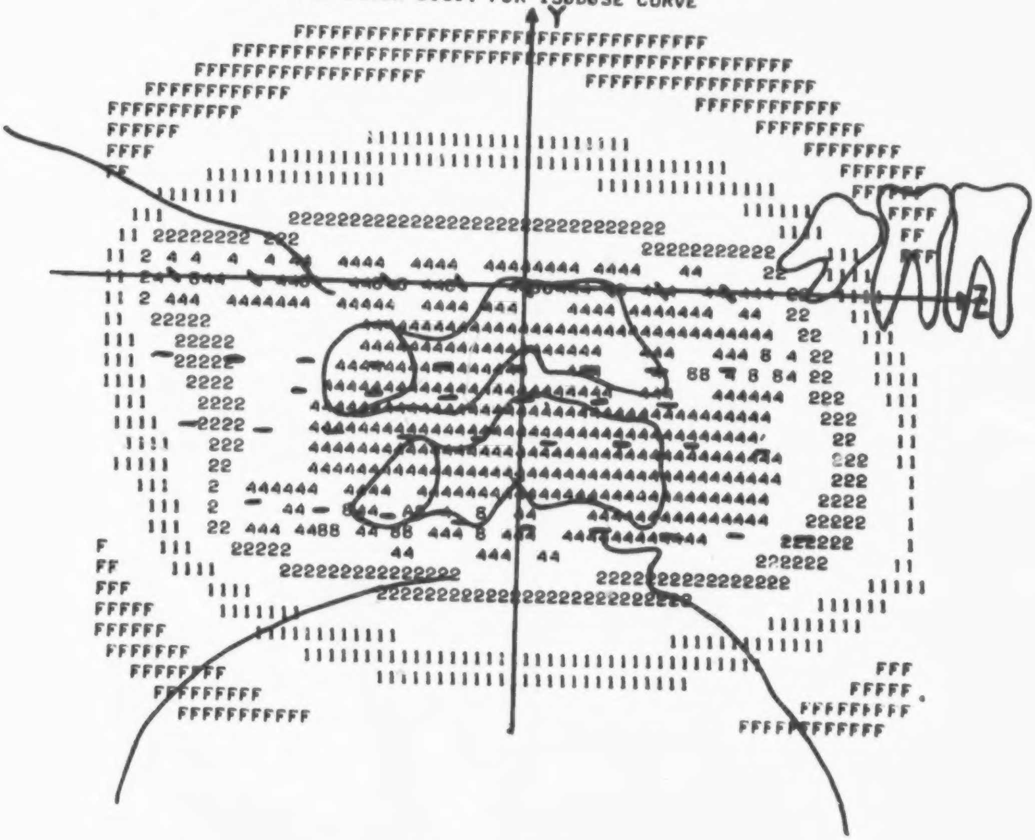


Figure 4. Computed dose distribution in lateral plane parallel to 6 ribbons of iridium 192 seeds.

```
DISPLAY CASE  CERVIX  RA-226

INVERSE SQUARE CALCULATION     :              SCALE              :
                               :---------------------------------:
Z = 0.0                        :    SYMBOL   :       RADS        :
                               :             :  FROM  :    TO    :
                               :-------------:--------:----------:
PROJECTION - - A.P.            :      F      :   500  :   707    :
                               :      1      :  1000  :  1414    :
                               :      2      :  2000  :  2828    :
                               :      4      :  4000  :  5656    :
                               :      8      :  8000  : 11313    :
                               :      A      : 16000  : 22627    :
                               :      *      : 32000  : MAXIMUM  :

               TRACE OUTER DIGIT FOR ISODOSE CURVE
```

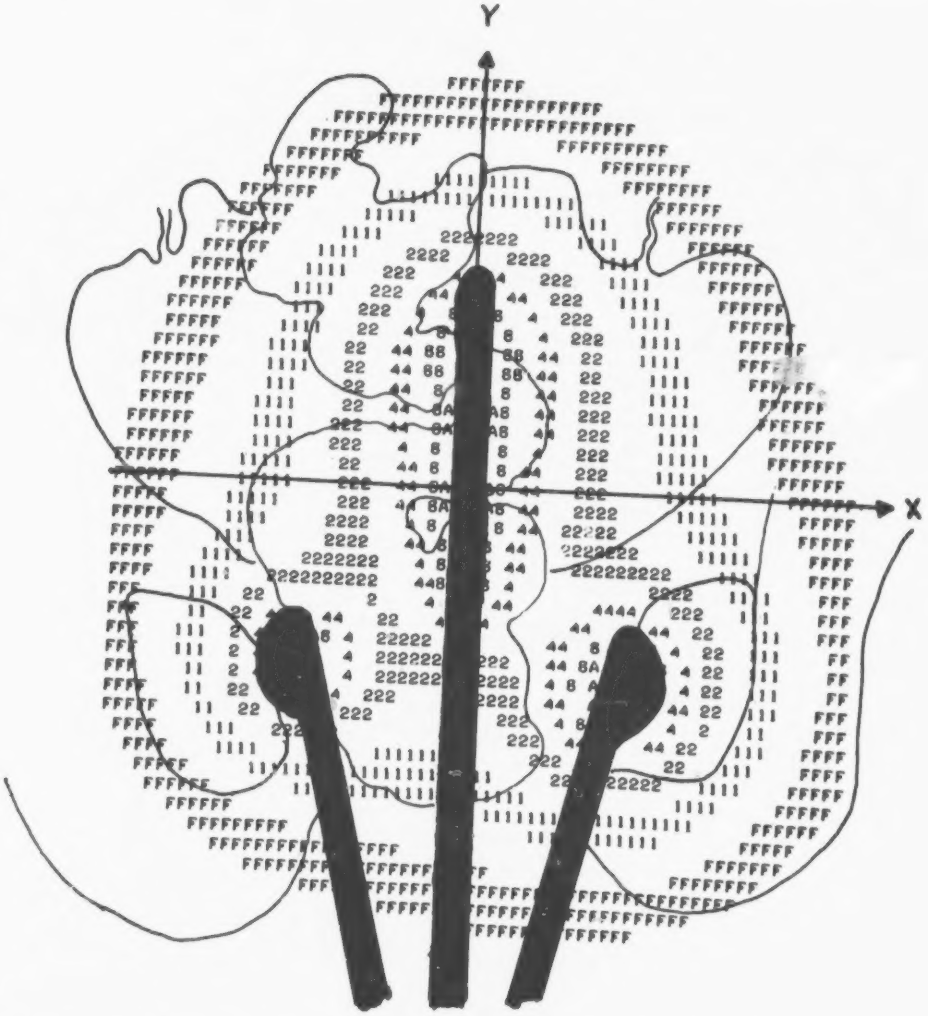


Figure 5. Automatically computed dose distribution for radium cervix applicator. An anterior projection is shown of plane containing the tandem and ovoids.

```
DISPLAY CASE   CERVIX   RA-226

INVERSE SQUARE CALCULATIØN     :              SCALE               :
                               :----------------------------------:
Z = 0.0                        :   SYMBØL   :        RADS         :
                               :            :   FRØM  :    TØ     :
                               :------------:---------:-----------:
PRØJECTIØN - - Lateral         :      F     :   500   :   707     :
                               :      1     :  1000   :  1414     :
                               :      2     :  2000   :  2828     :
MAGNIFICATIØN - 1.36           :      4     :  4000   :  5656     :
                               :      8     :  8000   :  11373    :
                               :      A     :  16000  :  22627    :
                               :      *     :  32000  :  MAXIMUM  :
```

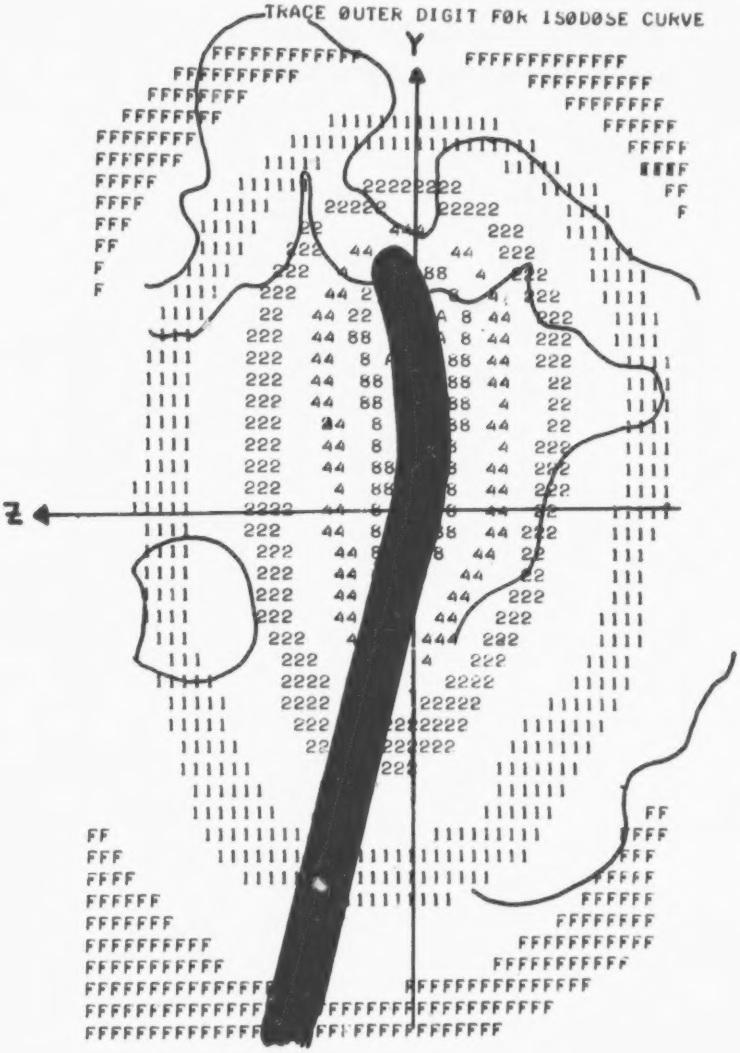

TRACE ØUTER DIGIT FØR ISØDØSE CURVE
Y
Z

Figure 6. Lateral projection of removable radium insert in cervix with dose distribution.

```
                    DISPLAY CASE   I-125   LEFT LUNG
IODINE TABLE CALCULATION      :             SCALE               :
                              :---------------------------------:
ITABZ = 3.33                  :  SYMBOL   :        RADS         :
                              :           :  FROM  :    TO      :
                              :-----------:--------:------------:
PROJECTION - - AP             :     F     :   500  :   707      :
                              :     1     :  1000  :   1414     :
                              :     2     :  2000  :   2828     :
MAGNIFICATION = 1.27          :     4     :  4000  :   5656     :
                              :     8     :  8000  :   11313    :
                              :     A     : 16000  :   22627    :
                              :     *     : 32000  :  MAXIMUM   :

                   TOTAL DOSE DELIVERED OVER ONE YEAR

                   TRACE OUTER DIGIT FOR ISODOSE CURVE
```

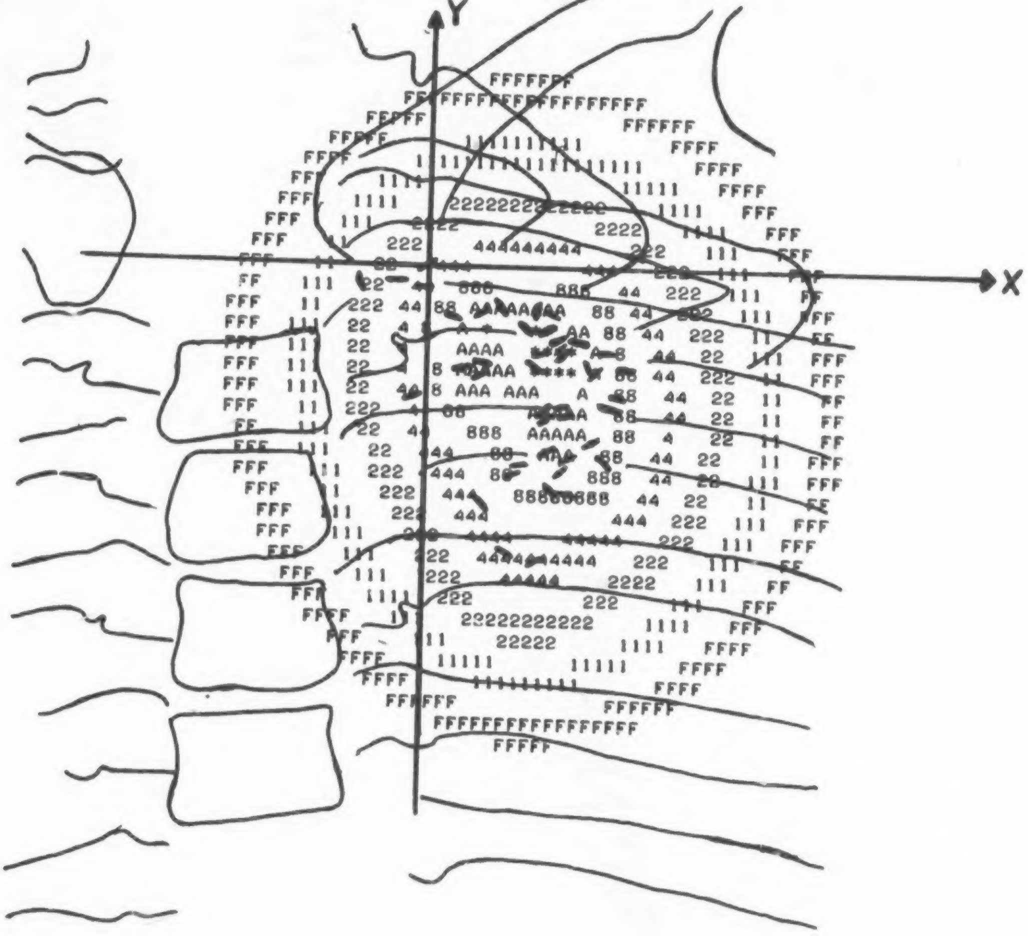


Figure 7. Anterior projection of iodine 125 seed implantation of a mediastinal mass for which the dose distribution analysis was carried out by automatic computation with the MIDAS program.

```
              DISPLAY CASE   I-125   LEFT LUNG

IODINE TABLE CALCULATION         :             SCALE              :
                                 :--------------------------------:
ITABZ =-1.78                     :  SYMBOL     :       RADS       :
                                 :             :  FROM  :   TO    :
                                 :-------------:--------:---------:
PROJECTION - -                   :     F       :   500  :   707   :
                                 :     1       :  1000  :  1414   :
                                 :     2       :  2000  :  2828   :
MAGNIFICATION = 1.28             :     4       :  4000  :  5656   :
                                 :     8       :  8000  :  11313  :
                                 :     A       : 16000  :  22627  :
                                 :     *       : 32000  : MAXIMUM:

                 TOTAL DOSE DELIVERED OVER ONE YEAR

                 TRACE OUTER DIGIT FOR ISODOSE CURVE
```

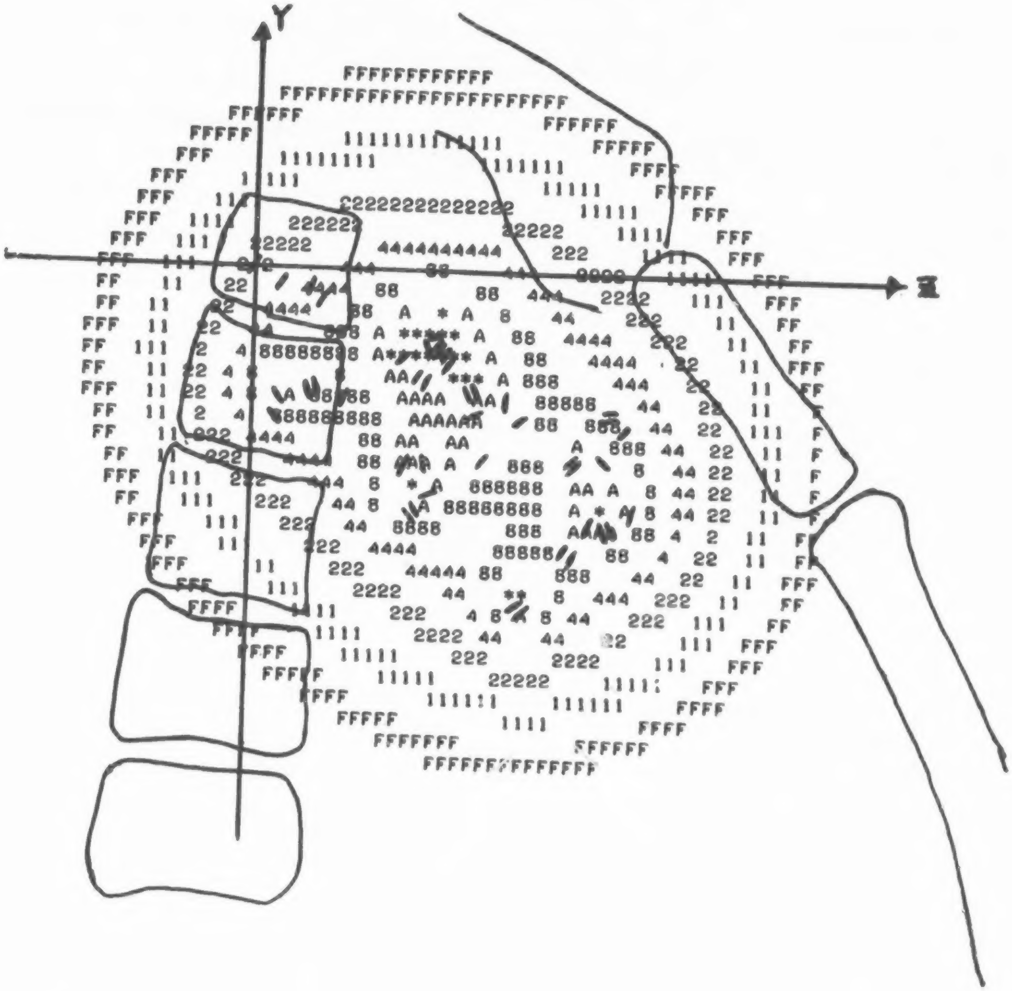
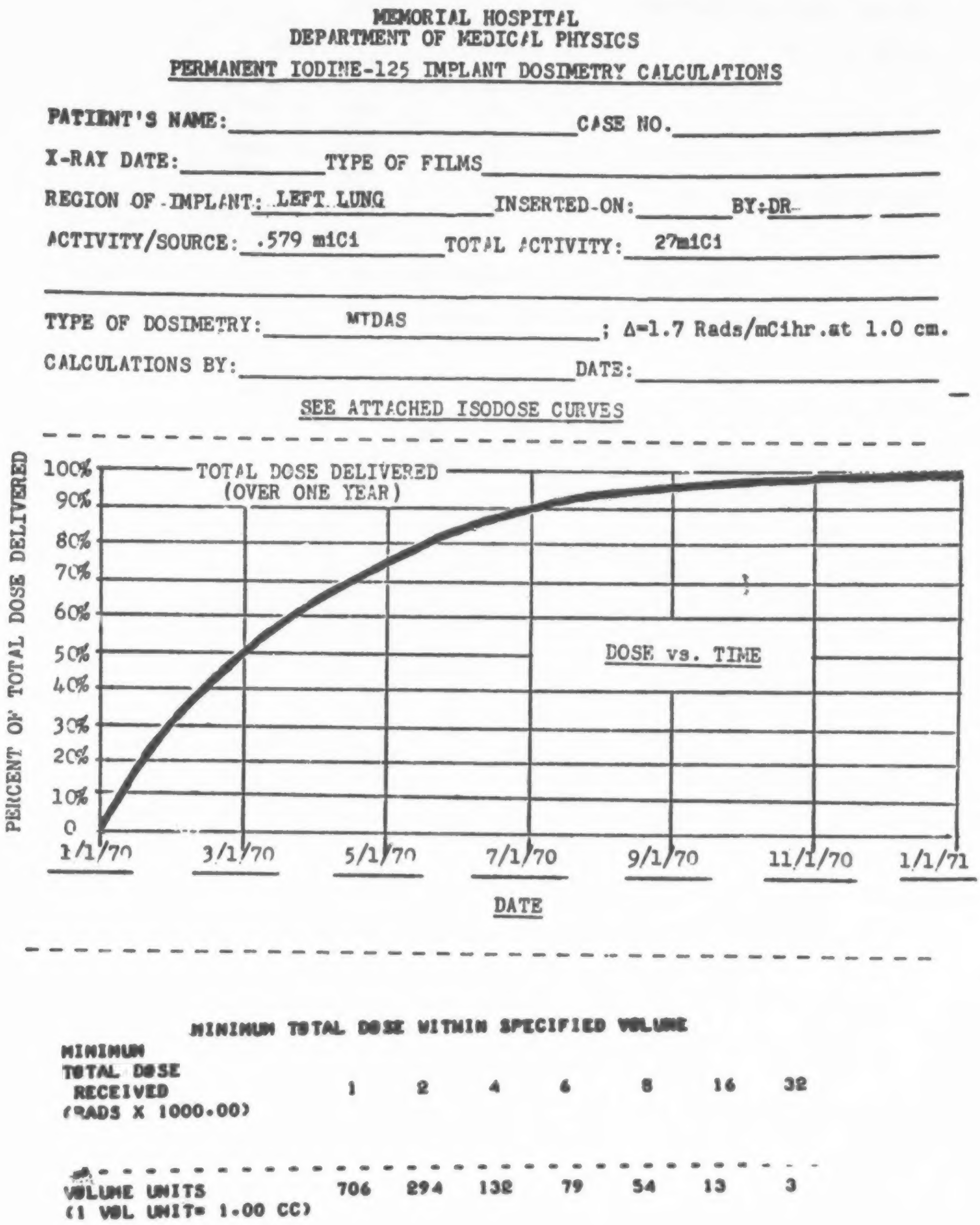


Figure 8. Lateral projection of iodine 125 seed implant with calculated dose distribution.



MEMORIAL HOSPITAL
DEPARTMENT OF MEDICAL PHYSICS
PERMANENT IODINE-125 IMPLANT DOSIMETRY CALCULATIONS

PATIENT'S NAME: CASE NO.

X-RAY DATE: TYPE OF FILMS

REGION OF IMPLANT: LEFT LUNG INSERTED ON: BY: DR

ACTIVITY/SOURCE: .579 mCi TOTAL ACTIVITY: 27mCi

TYPE OF DOSIMETRY: MTDAS ; Δ=1.7 Rads/mCihr.at 1.0 cm.

CALCULATIONS BY: DATE:

SEE ATTACHED ISODOSE CURVES

TOTAL DOSE DELIVERED
(OVER ONE YEAR)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0
PERCENT OF TOTAL DOSE DELIVERED
DOSE vs. TIME
1/1/70
3/1/70
5/1/70
7/1/70
9/1/70
11/1/70
1/1/71
DATE

MINIMUM TOTAL DOSE WITHIN SPECIFIED VOLUME

MINIMUM TOTAL DOSE RECEIVED (RADS X 1000.00)	1	2	4	6	8	16	32
VOLUME UNITS (1 VOL UNIT= 1.00 CC)	706	294	132	79	54	13	3

Figure 9. Portion of dosimetry report on iodine 125 seed implantation showing accumulation of dose with time, as well as volume dose analysis.

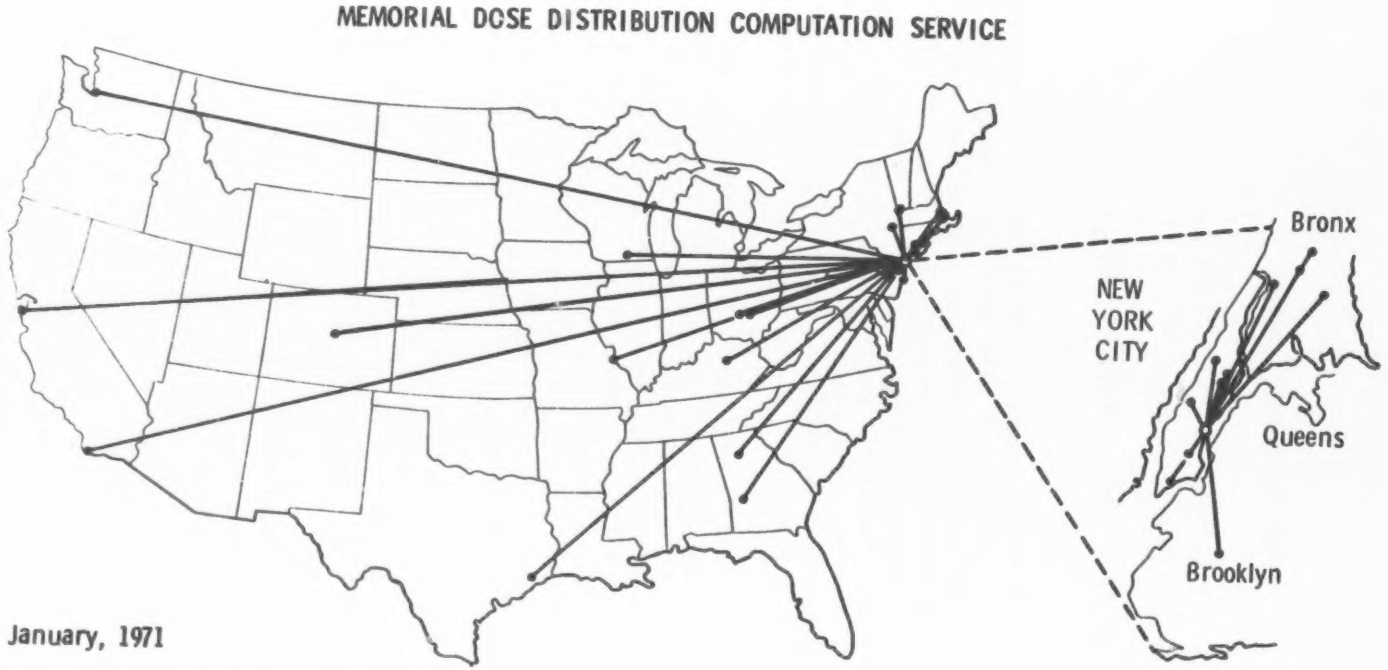

MEMORIAL DOSE DISTRIBUTION COMPUTATION SERVICE
NEW YORK CITY
Bronx
Queens
Brooklyn
January, 1971

Figure 10. Location of 30 of the 37 hospital therapy departments that utilize the Memorial Dose Distribution Computation Service.

THE MANCHESTER SYSTEM

H. M. Parker, M.Sc., F.Inst.P.

The hyphen got into the Paterson-Parker relationship in the fall of 1932, so this "prehistory" will date from that time. It would be grossly unfair to Dr. Paterson and his clinical colleagues, or for that matter to equally distinguished groups elsewhere, to imply that this hyphen caused a quantum jump in the success of radiotherapy. At the time, there were several effective centers for radium treatment. Both the distribution of radium sources and the "dosage" of radium had been empirically developed, so experienced therapists had a good feeling for a sensible approach to treatment.

For example, for surface applicators, the Brussels system of Murdoch, Simon, and Stahel was a highly successful combination of medicine and physics, because this team was willing to spend literally days in empirically adjusting sources and making hand calculations to get even irradiation. I have often speculated that if computers had been available at that time to do the calculations in minutes or seconds rather than hours, we might have stayed with their methods. In fact, I sometimes suspect now that we have such computers some clinics are almost going back to that approach.

The basic purpose of the Paterson-Parker system was to permit derivation of a sound distribution of radium sources for effective treatment over the prescribed tissue region, and to know the dose without each clinician having to repeat the learning curve of experience.

The "distribution" part of the work is the more interesting, so let us get the primary dose method out of the way first. The time was 1932, 4 years after the introduction of the roentgen for x-ray doses. Contemporary attempts to correlate radium gamma ray measurements with the more conventional x-rays measurements were fascinating, but not always convincing.

We took a method which, in the physics of the time, would have been called a derivation of Eve's Number. (Dr. Eve had a daughter

"Millie Eve" and his contributions certainly merit having the units eve and milli-eve in literature.) The experiments we used were those of L. H. Gray in which he measured the energy absorption, as determined by ionization, in a large graphite block surrounding a radium source. We derived a so-called K value of 9.3 R per hour. As more generally applied, we used 8.4 R per hour through 0.5 mm Pt filter. Probably the best measurements today would give about 8.25 R per hour.

You may have seen a paper by E. H. Porter in BJR (September 1970) entitled "How many rads per Paterson-Parker roentgen?" The question should be "How many roentgens per rad?" Our derivation was a Bragg-Gray Principle application before L. H. Gray became interested in hospital physics (eventually becoming one of the world's best, if not the best) and also, of course, before the prior statement of the Principle by Bragg (1912) had been resuscitated.

Enough about dose. From the one figure for the dose-rate at 1 cm from 1 mg of radium, it is simply an exercise in the inverse square law to determine the dose from any configuration. This is the essence of the intensity-millicurie hour (Imc-hr) system of Sievert.

Let us now return to the distribution problem. The work started with surface applicators. Distribution patterns were best known for uniform circular rings of radium. Since many surface lesions are more or less circular, it was natural to develop simple arrangements of multiple concentric rings to achieve surface homogeneity of dose, accepting a purely arbitrary variation of ± 10 percent over the treated area.

Obtaining a flat distribution on the surface was somewhat of an obsession, perhaps because in 1932, the skin, was the principle barrier to getting enough radiation to all needed parts. Of course, one never really treats a "surface." There is always some sort of volume to be considered, depending on the thickness of the tumor. In retrospect, it is a curious omission of the Manchester System that no simple rules for assuring adequate uniformity in depth were given. I was quite shaken, when putting these notes together, to discover how cavalierly we had dismissed this point. To quote:

"In planning skin applicators, or dental molds, an attempt is made to treat an area at least one or two centimeters wide of apparent tumor, and to use a distance which will give adequate dose at sufficient depth."

Translation: "When I say 'adequate' and 'sufficient' I know what I mean, and you should, too!" However, if you rework the original examples given, you will find stated depth doses in the range of 56-72 percent. If we had specifically addressed ourselves to the problem, I suspect we would have said that the depth dose at the greatest depth needing treatment should not be less than 80 percent of the calculated surface dose. The worked examples give depth doses with a safety margin of depth, just as we had taken a margin in the radius.

Once we had worked out the flat system for circles, the next step was to do it for squares, not because squares are the next "logical" shape--ellipses might perhaps have been that--but because we had field distribution data for lines of any length, courtesy of Dr. Mayneord for unfiltered sourses and Dr. Sievert for sources requiring oblique filtration corrections. There is no logical relationship between the patterns for compound circular applicators and for the squares with added "lines." We simply took existing practice and found a reasonable value for the maximum spacing of lines (2h), and for their linear activity relative to the periphery.

The arrangements got interesting when we found that the same dose came from equally loaded squares or circles of the same area. It followed that a common dose curve would do for any area, with a rather small correction for elongation.

Extending the argument to curved surfaces was the next obvious step. The device of calculating for the "area treated" for convex surfaces and the "area of the applicator" for concave surfaces is about as arbitrary and empirical as one could get. It just happens to work in most cases. If we had a computer to run out many more cases in detail, we might have been discouraged and missed the practical simplification!

In the interest of time, I will skip what the Manchester System did with cylindrical applicators and with uniform dose surface ovoids for cervix treatments.

The systems for interstitial therapy were decidely more interesting. We tried innumerable ways to come to some volume dose system by combinations of the existing plane figures--none showed us the generalizations we needed. We had to go back to the elegant solution of Souttar for the case of a sphere with two zones of hypothetical radioactive fluid which we later called the rind and core.

In nearly all branches of science and technology, there are some practitioners whose contributions do not make the impact on the literature that they should have. Souttar was a bioengineer decades ahead of his time. While practicing as a highly respected clinician, his mind was that of a first-class mathematician.

It was Souttar who finally persuaded me that there was no alternative but to extend the simple mathematics of the sphere to all required shapes. Only the sphere could be done as a perfect integral, all the rest required laborious numerical integration. I spent the greater part of a year on this. A few years ago, I had my computer associates estimate what it would take on a computer--about 2 minutes was the answer--so we have made some progress. However, the work was fun for its time, as it led to the one simple formula to treat a volume (V) of any reasonable size and shape:

$$M= 34.1\, V^{2/3}\, e^{0.07\, (E-1)}$$

As a minor historical note, I think I derived a completely disproportionate satisfaction from the purely empirical elongation correction. Perhaps it was some compensation for dreary hours of calculation to contemplate that a cigar body whose length is 10 times its diameter gives the same dose, when treated on the two-shell principle, as a discus whose diameter is 10 times its thickness, when both are adjusted to the same volume and radium content, provided that the radium is properly spread on the rind and core principle.

All parts of the Manchester System were made to apply generally, regardless of scale, by ignoring scattering and absorption of the gamma radiation in tissue. A number of people have worked on this phase, with results that are not in notably good agreement. Our own measurements, which were quite extensive, have never been published. We made measurements with condenser chambers that were quite small for their time--22 cubic mm. We also made some of the best "mathematical" sources, such as rings, by mounting a single gold seed on a minimally scattering lathe device and rotating the source. The chamber was arranged for measurements on any traverse of the configuration. By a slow rotation through 270° we could also do three-quarter circles and other configurations that were very hard to calculate. Until I looked at my 1934 notes I didn't realize that I had checked some of the convex surface applicators by having the chamber free to turn on an arc to describe the curved surface.

My tissue absorption measurements were second class in that it was inconvenient in my horizontal axis device to use water as the tissue substitute. Plastics of that period were not up to present day standard and tissue equivalents. Some measurements of that time implied about a 4 percent absorption and scattering in tissue per cm. I could never approach so high a value, which would have required corrections for large applicators and large volume implants. I was particularly pleased to see Miss Stovall's figure of 1 percent per cm, as that is about what I got with the prehistoric methods.

In volume implants bigger than any clinically used I found, with tissue added, a slight increase in dose in the central region and a slight decrease near the periphery. This seemed to be consistent with scattering theory. A contributing reason often is overlooked. In any implant, the dose received at any point comes very largely from the nearest sources. Those sources far enough away to suffer appreciable tissue absorption already are done in by the inverse square law.

However, these are antique measurements, and after 35 years we have better instruments, better materials, and better physicists which together can give superior answers on these points.

THE DEVELOPMENT OF RADIUM DOSIMETRY

Edith H. Quimby, Sc.D.

Radium was used in therapy within a few years after its discovery, but treatments were empirical. Each user worked out his schedule of application by trial and hope. The actual radium content of a given tube was known only roughly, based on the stated number of milligrams of radium salt, but the salts usually were impure and comparison from one source to another meant little. In 1911, Mme. Curie prepared a sample of a carefully weighed and analyzed radium salt which was deposited in the International Bureau of Weights and Measures near Paris. Standards in all countries have been established by comparison with this, on a basis of some measure of the radiation emitted. Since the number of milligrams of radium in the standard source is known, other samples can be specified in terms of actual radium content.

A certain number of milligrams of radium always emit the same amount of radiation per unit time, so treatments came to be specific in terms of milligram-hours. By itself, this statement obviously is meaningless. The effect to be expected from a certain number of milligram-hours depends on the distance of the source from the irradiated region, the filtration, and the size and shape of the applicator within which the radium is distributed. Each doctor determined for himself the effect to be expected from any one of his sources at a definite distance and for a definite time. However, comparison of the effects to be expected from different applicators, or from similar applicators used by different people, was almost impossible.

Furthermore, it was realized that a specification of the number of milligram-hours, filter, and size and shape of source contains implicitly a statement of the energy leaving the source, which we call the emitted dose. However, the quantity arriving at the region to be affected, the delivered dose, may be a very small fraction of the energy emitted, and the actual absorbed dose that produces the biological effect can be even smaller. In 1919, Regaud (1), the leading French doctor in the field, called attention to these differences, pointing out that the absorbed dose was the information to be desired, but confessing that at that time the only unit he could use was milligram-hours.

Others began to be disturbed by the lack of means for standardizing dosage, and of any practical method to correlate the work of different radium therapists. Since biological reactions were to be observed, it seemed that a biological dose unit might be desirable, and various were proposed. The first probably was that of Russ (2) who in 1919 proposed using the amount of radiation necessary to kill mouse cancer. This was to be determined experimentally and called -- interestingly enough -- the rad. Various others were proposed; perhaps the most practical was the amount to produce an erytherma on human skin. But the use of any such reaction as a unit is quite impractical. An almost infinite number of values would have to be determined experimentally for every practical combination of milligram-hours, distance, filter, etc. No reference standard could be set up and kept for use by individuals from different institutions, for instance.

One system that offered promise was determination of the darkening of photographic film by the radiations. From the middle 1920s on, a number of investigators employed it in various researches. Within considerable limits, the degree of darkening is proportional to the amount of radiation producing it, so long as the quality of the radiation, the nature of the film, and the details of the development are unchanged. Standard procedures can be set up for calibration. (This essentially is the basis for film badge monitors at present.) Variations of opacity in a piece of film resulting from a single exposure can be studied almost from point to point, giving a good idea of the distribution of the radiation around a source. Pieces of film can be placed within blocks of material serving as a phantom, to investigate dose distribution within the body. In many ways this has been a useful technique. However, as a basis for standardization, it became evident that too many variables were involved.

Evidently, a basic physical standard was desirable. If such a unit could be established, its relation to expected biological effects could be determined; but there would always be the basic physical standard to go back to.

The most direct measurement of energy absorbed by tissues in any given situation would be the amount of heat generated by this absorption in the region under consideration. In 1913 Rutherford and Robinson (3) made the first attempts to measure the heat resulting from the absorption of radium radiations in a solid. Many others have studied it since. They were in general determining the result of total absorption of the radiation, not the part absorbed in a small region. Calorimetric measurements demand very carefully constructed apparatus and sophisticated experimental procedures. Early results varied greatly among investigators. However, fair agreement finally was obtained for the total energy absorption. Efforts were made to develop small calorimeters for the local problems, but for many years this seemed hopeless. Now microcalorimeters have been developed and interesting results obtained, but even now they have little use in practical dosimetry.

To the physicist, of course, the erg as the unit of absorbed dose seems straightforward. Such a unit could readily be defined, but its actual realization was difficult. As early as 1905 Eve (4) suggested an indirect approach to this problem: determination of the number of ion pairs produced during the absorption of the radiation, and determination of the energy absorbed per ion pair. This is, in fact, essentially the basis of present-day methods. In the early years, however, nothing satisfactory came from this work; the experimental difficulties were too great.

In 1921 Failla (5) attempted the first calculation of absorbed energy based on available information in the literature. By this time a good deal of information was available about the total energy emitted by radium or radon, and its partition among alpha, beta, and gamma rays. Also, absorption coefficients for the radiations in water had been published. From such data and some geometrical considerations, he calculated the microcalories absorbed in a piece of skin 1 square centimeter in area and 1 mm thick, for therapeutic procedures with different applicators in use at the Memorial Hospital in New York. Each of these treatments produced a faint but definite erythema on the skin under the applicator. The values for energy absorbed averaged about 400 microcalories in one-tenth of a gram of tissue. (This is about 1,700 rads, which would be expected to produce a definite erythema. Considering all the approximations involved in the calculation, the agreement with present-day data is remarkable. It took the experts 30 years more to invent the rad and specify its use.

In the decade of the 1920s the roentgen had been established as the unit for x-rays in the 100-200 kilovolt region, and standard and secondary ionization chambers were developed for its measurement. None of these instruments, however, was suitable for use with radium, particularly considering the small source sizes and short distances usually involved. In an ionization chamber 1 cm in diameter so placed that its center is 1 cm from a small radium source, the intensity of radiation in the portion of the chamber nearest the radium is approximately 9 times as great as that in the opposite portion; so the actual ionization recorded means little. Yet in interstitial therapy, it is just such short distances that are important. Ionization measurements continued to be investigated, but it was not until the late 1930s that successful basic procedures were established.

Concurrently with various experimental efforts to arrive at measurement of radium dosage, a good deal of radium and radon therapy was being done with various types of sources, the suitable clinical exposure being determined by trial. It was highly desirable to have some method of comparing "doses" from these sources and from new ones that might be produced. Since no satisfactory measuring instruments had been developed, our group at the Memorial Hospital found it expedient to develop a simple mathematical method for dosage determination (6, 7). A full-size diagram of each source was made and divided into a number of small parts, each of which could be considered as approximately a point source. For a particular source-skin distance, the distance of each small element from the central point on the skin was calculated. The effect of additional filter because of the oblique passage of the rays through the container was also calculated. The sum of the contributions of the separate elements gave the dose, in arbitrary units. For convenience, doses delivered by all sources were related to that from a point source at 1 cm distance. The tables thus developed contained data for about 200 practical applicator sizes and distances. (Remember, this work was done when the only computer available was a slide rule.)

Now if the number of milligram- or millicurie-hours required to produce any specified reaction with any listed applicators is known, the number required for any other applicator can be determined. Calculations were made only for filtration of one-half mm of gold or platinum, since this removes all the beta rays and transmits the maximum amount of gamma. Thinner filters, or filters of silver, steel, monel metal, etc. were too variable to permit definite study; in any case, they usually were enclosed in enough secondary material to bring them to essentially the gamma level. Thicker filters reduced the amount of gamma rays transmitted, without altering the pattern of penetration in a few centimeters of tissue. For those using heavier filter, a correction factor was supplied.

In subsequent years other groups published similar tables, which are all in good agreement. The Paterson-Parker system, the one most widely used for the past 30 years, will be discussed in the next paper, so I will not spend time on it here.

Continuing efforts had been made to measure radium gamma-rays in terms of roentgens. When fairly large sources were available, so that reasonable source-to-ion chamber distances could be used, it was hoped that the standard open-air chambers used for x-rays in the 200 kilovolt region, might prove satisfactory. Using chambers that produced concordant results for x-rays, physicists obtained values varying from 2 to 8 roentgens per mg/hr from "point" sources of radium at a distance of 1 cm. Measurements were made at greater distances and with sources of different sizes, of course, but no set of corrections could be devised that would bring these values into harmony.

It finally was recognized that the troubles had to do with secondary electron equilibrium. There is no time to go into details but after the difficulties were recognized and coped with, values in the neighborhood of 8.4 roentgens per mg hr were obtained. This value has been widely used as the radium emission constant, though recent refinements in measuring procedures have given a value of 8.25, which is presently accepted as correct.

Using this value in the calculated tables, it is now simply a matter of mathematical conversion to express doses from all the applicators in terms of roentgens. However, these are still only doses delivered. To find the absorbed dose, it is necessary to determine what part of the arriving energy is actually absorbed in the tissue. The absorbed dose is specified in ergs per gram; the unit, 1 rad is 100 ergs absorbed per gram of any absorber. The determination of rads absorbed per roentgen of exposure depends, in a complicated way, on the energy of the radiation and the nature of the absorbing material. For relatively low energy x-rays, for instance, the absorption coefficients for soft tissue and bone vary greatly; rads per roentgen in bone may be several times as great in soft tissue. This difficulty does not arise with the penetrating gamma rays of radium. Average values give 0.96 rads per roentgen for soft tissue, and 0.92 rads per roentgen for compact bone. Presently, published tables giving radium doses in rads are based on the soft tissue factor. For bone the correction of about 4 percent may be applied, although in view of other uncertainties it is insignificant.

In the treatment of patients, one thing becomes obvious: there is no one point at which dose designation is critical. Dose at the center of the tumor does not tell what is happening at the periphery -- often a more critical region. For many years, in gynecological problems, doses at points A and B of Tod and Meredith were cherished. But as the practice grew of taking radiographs of the patients with the radium in place, it was realized that these ideal points might very well not be where they were supposed to be. Various standardized systems of applicators grew up and isodose charts were supplied for the regions surrounding them. But again, when they were compared with the patients' x-ray films, they didn't fit. It now is realized that it is necessary to make three-dimensional radiographic examinations and calculate doses for many points, as they actually lie. This would be impossible without the use of computers, and Dr. Laughlin has told us of the wonderful studies that can be made with their aid.

In recent years, advances have also been made in the problem of meaningful measurements close to radium sources. Really tiny thermoluminous dosimeters can be used in close proximity to the sources. A large number of them can be used to map radiation fields in phantoms, and some may even be implanted in critical regions in the body to obtain a direct measurement of absorbed dose.

The rate at which the radiation is administered is important; and this, of course, does not appear in any dosage table. It is well known that recovery or repair takes place following a treatment, and that the amount of radiation delivered in fractionated or protracted treatments over a number of days will produce less effect than the same dose delivered at a single sitting. Various clinicians have determined the period they consider optimal, and state their dose as so many thousand rads delivered in so many days. But if another person is to achieve the same effect in fewer or more days, he must use fewer or more rads. This is an area which very little precise information is available. Various "recovery" curves have been published; they deal with specific tissues and, in general, with clinical reactions; information gained from them is suggestive rather than explicit, and little more is to be expected.

However, one point in relation to radium dosimetry should be made in this connection. When radium needles are implanted in a lesion, irradiation is at a constant rate for the 4 or 5 days they are in place. When radon is used instead, the time distribution for the same number of rads is quite different. Half the total dose is delivered in the first 3.8 days, three-fourths in a week, and the remainder at a constantly decreasing rate for the rest of a month. It would hardly be expected that the same result will be produced. The same considerations apply to any radionuclide left in the body for total decay.

As soon as we get into radiobiology, our accurate radiophysics obviously leaves something to be desired. Thus it appears that with each step forward in our dosimetry problem we discover another that needs to be tackled. Physics would seem to have gone about as far as it can; clinical experience alone is not enough; the engineers are helpful.

It will require pooling and careful analysis of all our knowledge to make the next steps.

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ABSORBED DOSE FROM INTERSTITIAL AND INTRACAVITARY SOURCES

Robert Loevinger, Ph.D.

This paper discusses a single aspect of the absorbed dose from interstitial and intracavitary sources: the dose to water as a function of distance from a point source of gamma radiation for various quantum energies. The water environment is assumed to be infinite, and the distribution of absorbed dose is then spherically symmetrical around the point source.

Radium is a logical starting point, since for many years interstitial and intracavitary therapy were carried out solely with radium or radon sources. It has long been known that narrow-beam attenuation for filtered radium gamma rays is about 2.5 to 3 percent per cm for water. (The value 0.028 cm^{-1} is commonly used for the narrow-beam attenuation coefficient.) It has also been known that scattered radiation approximately compensates for absorption near a filtered radium source in water; as a result, calculations of absorbed dose can as a first approximation, be based on inverse-square fall-off only to distances of about 10 cm of water. This information, known since about 1930, has been discussed and referenced in a review of radium therapy (1).

About 1950 various other radionuclides were introduced as sources for interstitial and intracavitary therapy. At the same time, experimental techniques for water-phantom measurements were being improved. Investigators made measurements for various radionuclides, using various detectors, of detector response as a function of distance from a small gamma-ray source in a water phantom.

At about the same time the radiation group at the National Bureau of Standards, under the direction of U. Fano, began systematic development of methods for computing the penetration of ionizing radiation in matter. This program soon led to many notable theoretical results, the most important for us here being the Spencer-Fano method of moments, which in turn was used in the Goldstein-Wilkins calculation of buildup factors. These and other results of that period have been reviewed and referenced in detail (2).

The part of the program of interest here is the calculation of the energy-absorption buildup factor in water. (The energy-absorption buildup factor is the ratio of the total absorbed dose at a point to the absorbed dose due to primary radiation alone at that point.) Energy-absorption buildup factors for water and tissue were later calculated by M. J. Berger of the National Bureau of Standards for the range of distances and quantum energies of interest in radiation medicine (3, 4).

A quantity closely related to the energy-absorption buildup factor can be determined experimentally using gamma-ray source and a large water tank. The experiment is carried out by mounting the source and detector inside the tank, and determining the ratio of the detector response in water to the response in air (in the absence of the water) for a fixed source-detector distance. The ratio must be corrected for any change in detector response due to change in spectral quality, and for the finite length of the source, in order to obtain the ratio of exposure in water to exposure in air at the same position for a point source of gamma radiation.

The various experimental studies of clinical-type gamma ray sources were compared with Berger's (at that time unpublished) results by Meisberger, Keller, and Shalek who in 1968 compromised between the experimental and theoretical results then available (5). These authors gave simple algebraic formulae to represent their judgment of the best values for clinical purposes.

Figure 1 gives the Meisberger, Keller, and Shalek results converted to dose to water per unit exposure in air (in rad/R). Their formulae were given in terms of exposure in water divided by exposure in air at the same point, and have been multiplied by the ratio

$$0.869 \frac{[\mu_{en}/\rho]^{water}}{[\mu_{en}/\rho]^{air}}$$

in order to obtain absorbed dose to water per unit exposure, measured in the absence of the water. For radium the calculated curve from Meisberger, Keller, and Shalek lies about midway between the broken line, which represents narrow-beam attenuation, and a horizontal line through the value 0.966 rad/R, which would represent the appropriate factor for simple inverse square fall-off only, without absorption or scatter. The solid curves shown were calculated from the equations recommended for clinical use by Meisberger, Keller, and Shalek, and also by Shalek and Stovall (6) in their recent survey of implant therapy.

Let us now go back a step. Using buildup factors calculated by Berger, the dose per unit of exposure can be calculated from the formula

$$\frac{D}{X} = 0.869 \frac{\sum a_i [(\mu_{en}/\rho) \exp(-\mu r)\ B_{en}(\mu r)]_i^{water}}{\sum a_i\ [\mu_{en}/\rho]_i^{air}}$$

This formula gives the dose D to water at a distance r from a point source, divided by the exposure X in air at the same distance from the point source. μ_{en}/ρ is the mass energy-absorption coefficient, μ is the linear attenuation coefficient, and $\beta_{en}(\mu r)$ is the energy-absorption buildup factor defined above. Numerator and denominator are separately summed over all gamma-ray energies, and a_i is the fraction of the total gamma-ray energy contained in line i. That is, $a_i = n_i E_i / \Sigma n_i E_i$, where n_i is the relative number of gamma-ray quanta of energy E_i emitted by the filtered source. Figure 2 shows the ratio D/X for monoenergetic point sources in water, for energies from 20 keV to 2 MeV. While from the viewpoint of interstitial therapy there is little interest in values beyond 10 cm, I have given values out to 20 cm in order to better illustrate the character of the curves.

The dose-to-exposure ratio is a strong function of both distance and quantum energy, and the variations are too great to be ignored in modern interstitial therapy.

The curves of figure 2 represent only a small part of an ongoing study of the interaction of ionizing radiation with matter now being carried out by the Radiation Theory Section of the National Bureau of Standards. The buildup factors on which these curves are based have recently been reexamined in order to assess the accuracy of the calculations. It is concluded that, for distances of interest in interstitial therapy, the buildup factor calculations are accurate to about 2 percent for energies above perhaps 100 keV, and perhaps a little less for lower quantum energies (7).

For monoenergetic gamma-ray sources, it is a straightforward matter to interpolate between curves of the type shown in figure 2. This has been done for 3 radionuclides of interest to interstitial therapy; the results are shown in figure 3, along with the corresponding curves calculated from the equations of Meisberger, Keller, and Shalek. These curves give the dose to water per unit exposure in air from a point source of the radionuclide, as a function of distance out to 10 centimeters.

While agreement between the two sets of data is reasonably good, the differences are greater than the uncertainty in the theory, and we might wonder as to their origin. It is seen that the agreement between the two sets of data is best between 2 and 5 cm from the source. In addition, it can be noted that the Meisberger, Keller, and Shalek formulae are in error in the limit of zero distance, since at these energies all the curves should have the same value there. It is my suggestion that the experimental data are least trustworthy at short distances, due to the finite size of the source and of the detector, and at large distances because of low detector response. I suggest that the theoretical curves shown as broken lines in figure 3 are the more trustworthy of the two sets of data. While the differences are not great enough to cause clinical problems, the numbers used in tissue-dose calculations might as well be the best available.

As a second use of the buildup factors, let us examine the useful distance of penetration into water for various quantum energies. The curves in figure 2 are readily converted into relative dose curves by multiplying by the reciprocal of the square of the distance from the point source. Dose curves in water of this type are shown (figure 4) for 20 keV, 200 keV, and 2 MeV, all 3 curves normalized to unity at a distance of 1 cm from the point source.

The purpose of these curves is to compare the dose distribution in water. To accomplish this comparison, we normalize the curves at a clinically interesting distance in water. It comes as no surprise to note that the inverse-square law dominates the dose curve from a point source. There are, however, real differences between the dose distributions for different quantum energies, and these are more easily seen by taking the ratio of the dose at each energy to the corresponding 2-MeV dose at the same depth, all normalized to unity at 1 cm.

The result is plotted in figure 5, where the relative dose ratio now is shown for several distances from a point source in water, and for quantum energies from 15 keV to 1 MeV. This figure tells us that for all energies above perhaps 0.6 MeV, the relative dose curves from a point source in water differ by only a few percent for distances out to at least 10 cm. Consider now gamma-ray quanta of energy about 100 keV. Figure 5 tells us that for distances greater than 1 cm, the relative dose curve lies above the 2-MeV curve, increasing to about 70 percent at 10 cm. For distances less than 1 cm the relative dose curves lie below the 2 MeV curve by about 15 percent at 4 mm, and by about 20 percent at 1 mm.

Consider now a quantum energy of about 30 keV. Figure 5 tells us that the relative dose curve for 30 keV differs by less than 10 percent from a 2-MeV curve from 1 mm out to 2 cm from the point source, and even at 10 cm the 30-keV dose has dropped only to 20 percent of the 2-MeV dose. This agrees with observations reported by the authors, suggesting the use of the 30-keV characteristic x rays of cesium 131 for interstitial therapy. They found a dose distribution in water comparable to that for radium, for distances out to 15 mm (8, 9). Similar use has been suggested for the 27-35 keV radiations from iodine 125.

The conclusions from figure 5 are not in agreement with implications of the statement in a recent review that "2 cm of tissue removes by absorption 50 percent of the radiation of iodine 125 and cesium 131" (6). The use of radionuclides with these low quantum energies does, of course, present difficulties regarding such matters as availability, cost, half-life, absorption in bone, penetration through metal filters, etc. However, insufficient penetration through tissue is not a reason for rejecting such sources.

In addition to information on tissue absorption, full information is available on the absorption of gamma rays in high atomic number materials. Thus, essentially all the physical information necessary for the dosimetry of gamma ray sources in homogeneous media is well in hand. Combine this with the general availability of computer techniques, and there no longer is any reason for the medical use of sources for which there is less than complete information on the distribution of dose in water or homogeneous tissue. It goes without saying that modern radiotherapy requires that the dose to tissue be expressed only in correct absorbed dose units (rads). From the viewpoint of the ability to express dose to tissue in rads, it makes little difference what quantum energy is used, from perhaps 25 keV to 2 MeV.

In order to make best use of the physical information now available for gamma ray sources, they should preferably be calibrated in terms of exposure (in roentgens). This can be done conveniently and accurately by comparison with a radium source calibrated in terms of quantity of radium, or by comparison with a cobalt 60 or cesium 137 source calibrated in terms of exposure. Use of the specific gamma ray constant to calculate the absorbed dose from a source (other than radon) which has been calibrated in terms of activity (in curies) is an indirect and unsatisfactory approach, liable to significant error.

Finally, a word about the comparison between theory and experiment. The uncertainty in the calculated buildup factors because of uncertainties in the cross sections and in the calculation is believed to be about 2 percent, at least for quantum energies above about 100 keV. The calculations were made with the simplifying approximation that the only photon interactions of importance are Compton scattering by free electrons and photoelectric absorption. Because of this approximation, it is estimated that the final uncertainty in the calculated buildup factor is perhaps 3 to 4 percent for quantum energies greater than about 100 keV, and perhaps a little more for quantum energies below 100 keV (7).

In my opinion, experimental determination of dose distributions around clinical gamma ray sources is likely to be less reliable than the calculated buildup factors. In order to be more accurate than the calculations, experimental measurements would require an accuracy of 1 to 2 percent for energies above about 100 keV, and a few percent for lower quantum energies. In places of using clinical-type sources, I believe it would be more useful to design a careful 1 percent experiment expressly to test the theory, especially for energies below 100 keV.

Such an experiment, contributing to information of general validity, would contribute more to accurate medical dosimetry than a series of measurements on clinical-type sources. Sophisticated theory and computational techniques have made obsolete any but sophisticated experiments.

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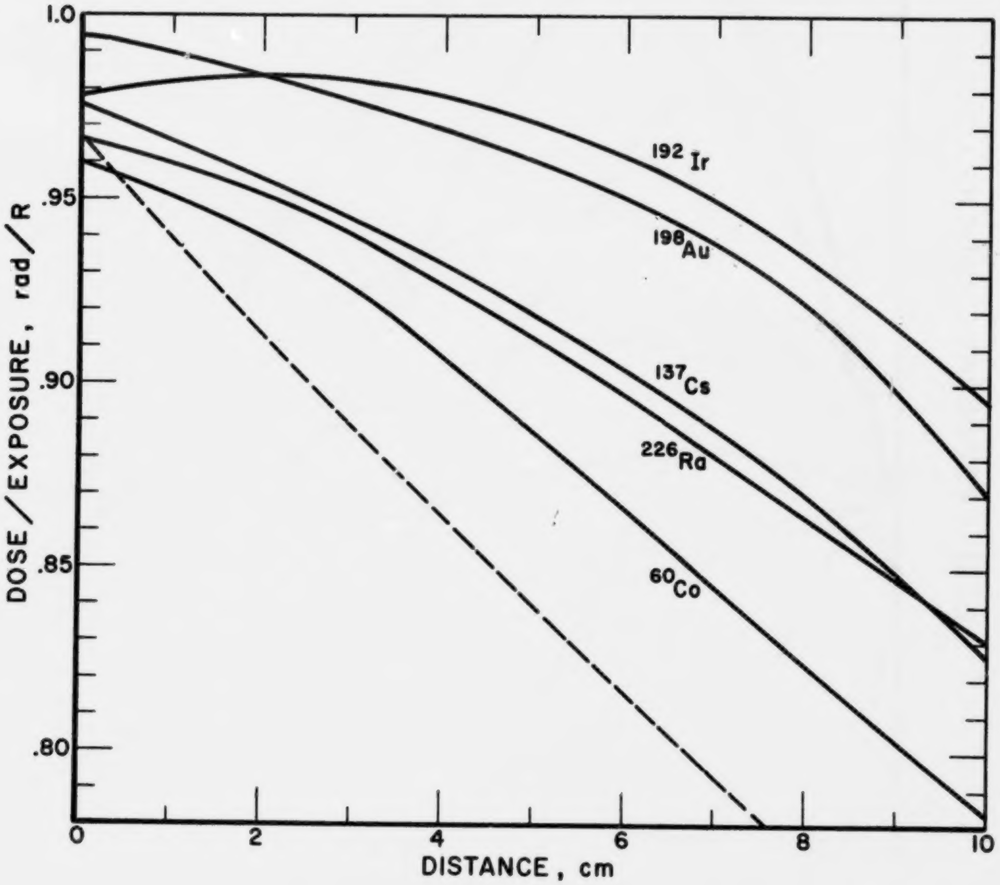

Figure 1. Dose per unit exposure vs. distance for a point source of gamma radiation in water. The ordinates give the ratio of the absorbed dose to water at a given point to the exposure in air at the same point in the absence of the water. The solid curves are calculated from the formulae of reference 5. The broken curve is calculated for exponential absorption with buildup, using the narrow-beam attenuation coefficient 0.028 cm^{-1}. In the absence of absorption and scatter, pure inverse-square fall-off alone would give the constant value 0.066 rad/R.

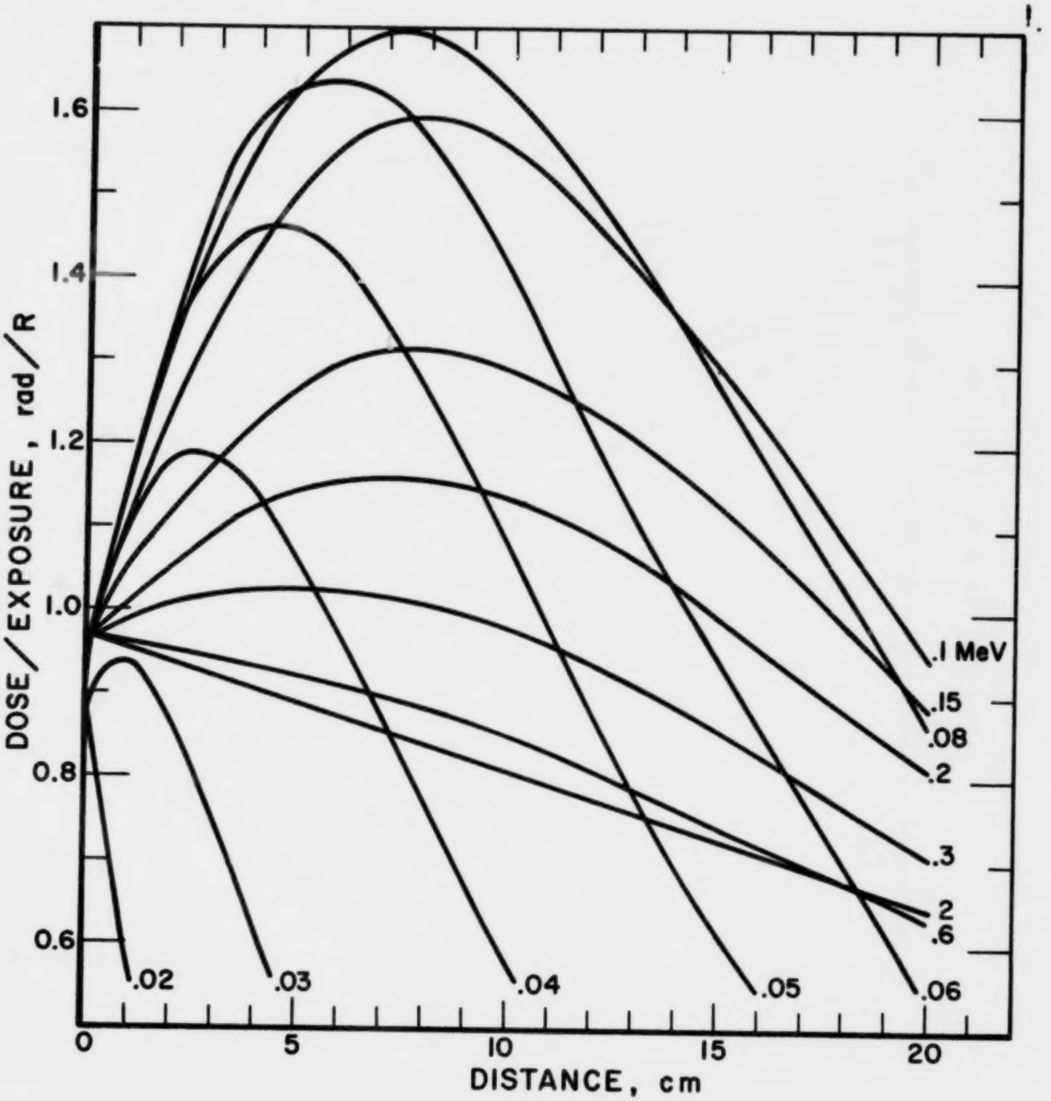

Figure 2. Same as figure 1. The curves are calculated from the buildup factors of Berger, as quoted in reference 3. For monoenergetic point sources with energies as marked on the curves.

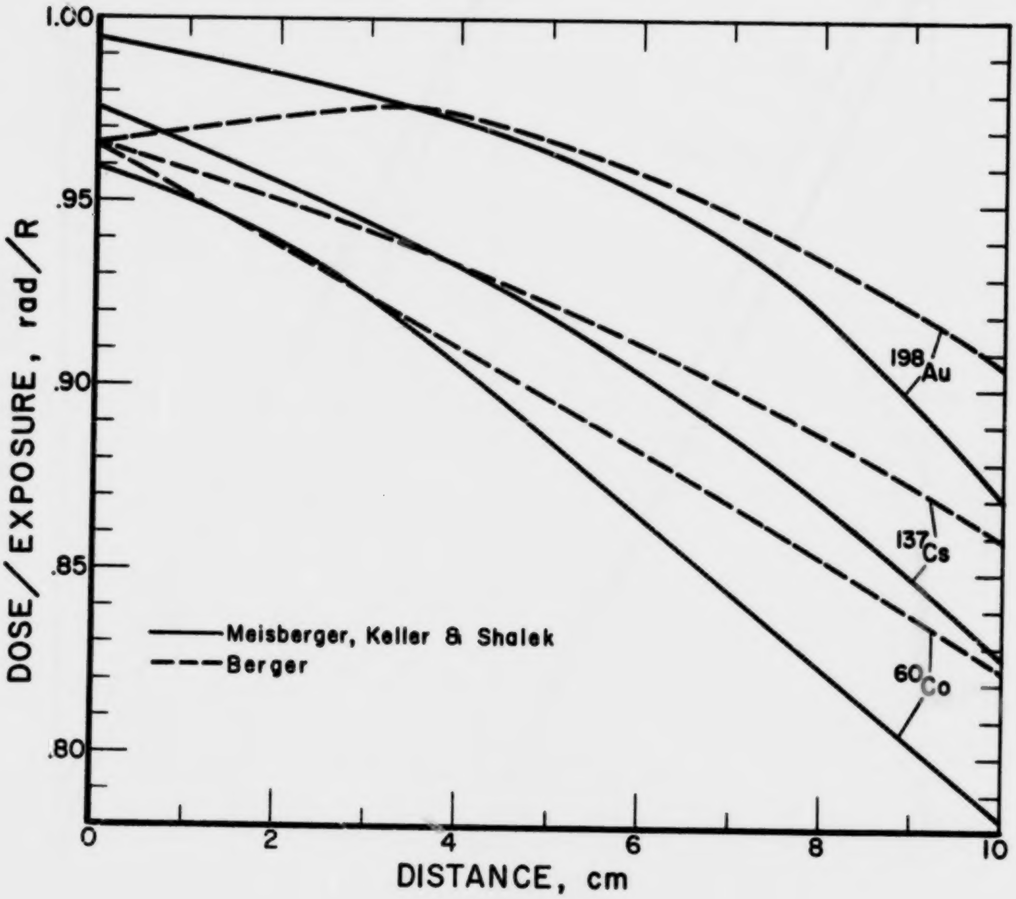

Figure 3. Same as figure 1. The solid curves are calculated from the formulae of reference 5. The broken curves are calculated from the buildup factors of reference 3.

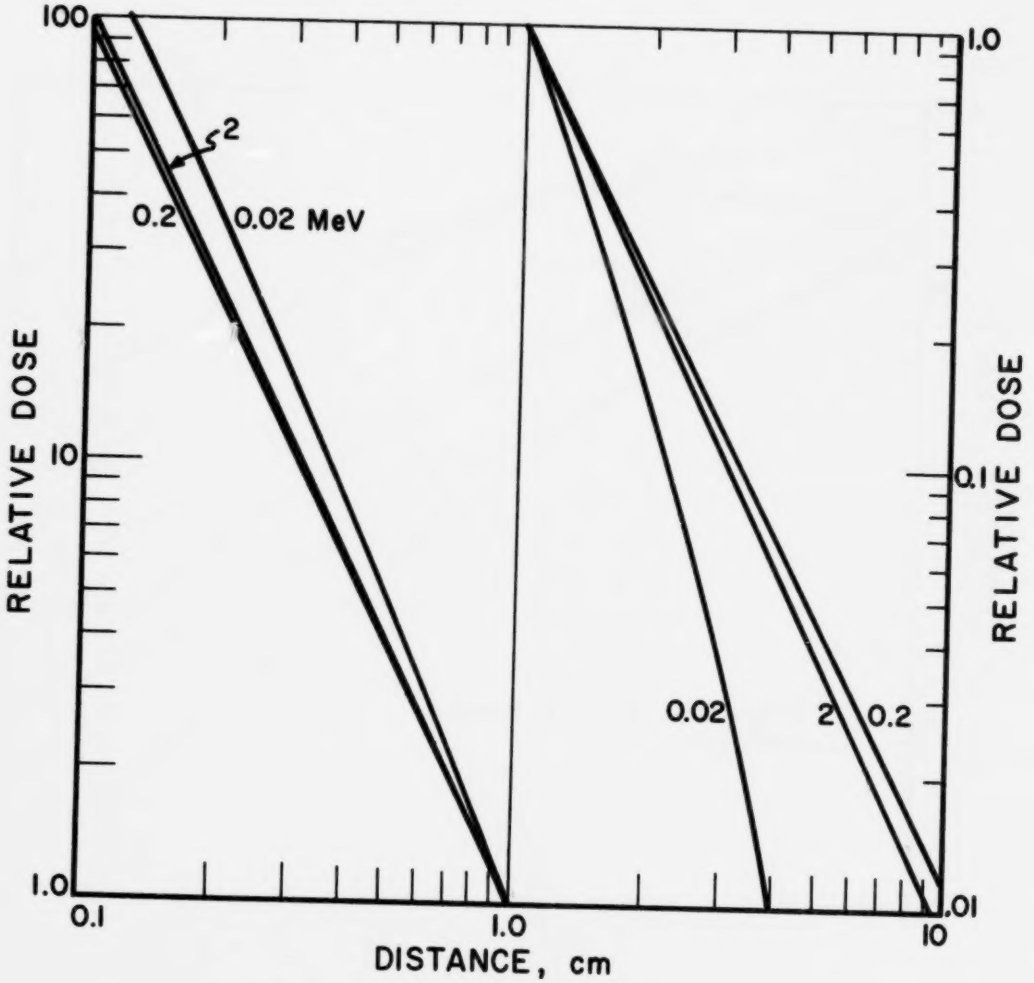

Figure 4. Relative dose vs. distance for a point source of gamma radiation in water. The curves for the 3 quantum energies indicated have been normalized to unity at a distance of 1 cm from the point source. The 3 curves on the left refer to the left-hand scale of ordinates, while three on the right refer to the right-hand scale of ordinates.

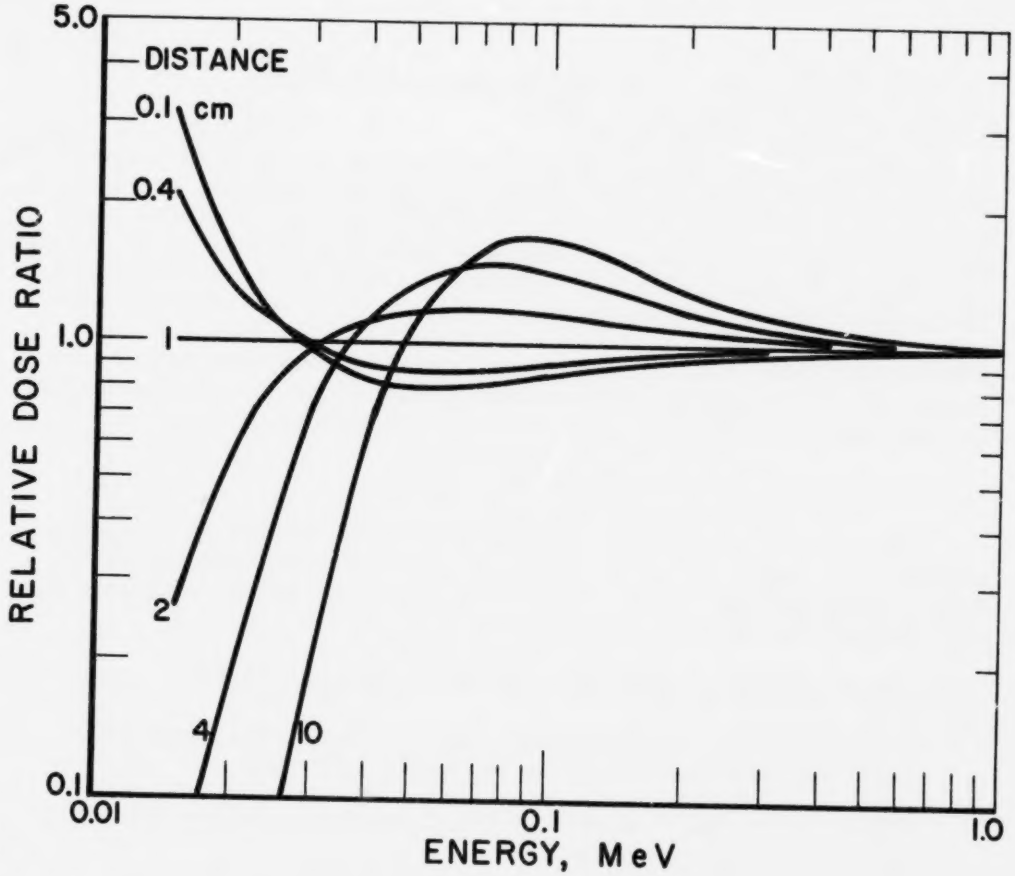

Figure 5. Relative dose ratio vs. quantum energy for a point source of gamma radiation in water. The curves give the ratio of the dose at a point to the dose at the same point from a 2-MeV source, with the ratio normalized to unity at 1 cm from the point source.

DOSIMETRY: THE RELATIONAL SYSTEM

Bernard Pierquin, M.D.

Although the final analysis of dosimetry is made from actual distribution of the radioactive material in the patient, it is necessary to develop a preliminary distribution chart to help the radiotherapist plan the optimum arrangement in given circumstances. Basic information for the preliminary distribution chart is developed in the present paper, and represents a systematic study of the dosimetry around one, two, or several straight parallel radioactive sources of equal length. Our presentation subsequently will be extended to cover varying clinical and geometric conditions, and rules for optimum distribution of the radioactive material.

1. Rules of the "Relational System"

These rules are based on the fundamental concept of relations between the length of radioactive sources and their spacing (1, 2). Before establishing them, it will be helpful to recall certain clinical factors and define certain terms.

Tumor volume: Volume of clinically apparent tumors.

Target volume: Tumor volume, plus an additional margin of surrounding normal tissue potentially involved.

Treatment volume: Volume of tissue with boundaries delimited by the minimum tumor dose.

Irradiated volume: All of the above, with surrounding normal tissues outlined by an isodose 50 percent of the value of the reference isodose.

Active length: The radioactive segment of the source.

Separation: The distance between sources, usually ranging from 0.8 to 2.1 cm.

Basic dose (B. D.): Established on a plane perpendicular to the radioactive sources, passing through the center of the target volume at the point (or points) equidistant from the lateral sources.

Reference isodose (R. D.): The isodose corresponding to the envelope of the treated volume. Its value varies according to the clinical and radiobiological conditions, and is about 85 percent of the basic dose. The minimum tumor dose is calculated from the reference isodose.

Overdosage isodose (2 R. D.): The isodose with a value double that of the reference isodose. It includes the area of overdosage around each radioactive source (figures 1-3).

The Rules

1. The radioactive material should be arranged in parallel and straight lines when possible. The direction of these lines defines the axis of implantation. Spacing between the different parallel sources should be as uniform as possible. (Anatomy in certain areas will impose variations and produce curved lines, curls, and nonparallel setups, such as triangles, which deserve special considerations.)

2. Continuity of the radioactive lines is indispensable in order to assure clinical and dosimetric control of the radioactive setup. Such continuity is accomplished either by use of continuous radioactive wires (iridium 192), or by an easily identifiable continuous framework such as cesium 137 seed carriers. (These methods permit localization of each radioactive line, either with televised image amplifier radiography or standard radiography and tomography.)

3. Each radioactive source should extend beyond the limits of the tumor volume in such a way that the minimal dose calculated at the reference isodose is attained over the entire area of the selected treatment volume. In practice, this insures that the radioactive wires protrude in each direction beyond the borders of the treatment volume, for a distance determined by the relation in size between the treated volume and the radioactive setup (see "Dosimetric Planning" below).

4. The separation between each wire will vary, according to the size of the treatment volume, between the following limits: 8-10 mm for a very small volume, 18-22 mm for a very large volume. These variations are necessary because of differences in the positions of the isodose around wires of different lengths (figures 4, 5).

5. The suggestion as to the spacing of sources must also take into consideration the tolerance to radiation of different tissues. The lower the tolerance, the smaller the separation between radioactive lines, in order to reduce the size of the overdosage zone in the immediate neighborhood of the radioactive wire.

6. The length of each radioactive wire is measured according to the exact requirements of the implant.

7. For straight lines, by reason of their being parallel, calculation of the dose can be made in a single plane perpendicular to the axis of implantation, passing through the center of the treatment volume.

8. This plane at right angles to the axis of implantation (after 3-dimension reconstruction or by tomography) shows each radioactive wire as a point (figure 6). The dose is calculated in the plane of cross section by means of standard circular isodose curves drawn around each point corresponding to a radioactive line, or inversely with the technique of "snail" isodose applied to each point of the tumor under study (figure 7 - 3, 4).

9. For a radioactive distribution in more than one plane, the minimal tumor dose rate is calculated for points equidistant between adjacent sources. Points on the periphery of the treatment volume with the same dose rate are located and a continuous line joining them is drawn, forming an isodose around the tumor volume. This is the reference isodose. Its value varies to around 85 percent that of the lowest point within the tumor, and it delineates the treatment volume. (The limits of the variations are defined by the appropriate radiobiological conditions in each case. They vary between 70 and 90 percent of the value of the base dose.)

10. The linear activity of the radioactive material in all wires within a given treatment volume is constant. In large treatment volume, spacing of lines of equal linear activity makes the dose in the middle of the implant higher than at the edges. This central overdosage is radiobiologically sound. On the other hand, it is always possible after appropriate calculation to remove a part of the radioactive material in the center of the treatment volume during the course of irradiation.

11. Linear activity is chosen so that the tumor dose rate (reference isodose) is about 30 to 60 rads/hour (about 750 to 1,500 rads/day).

12. Although one cannot fix a rigid upper limit to the tumor dose, we do not exceed 7,000 rads for a lesion treated solely by endoradiotherapy or plesiotherapy.

13. Biological consideration in a large treatment volume (integral dose) imposes an upper safety limit to the quantity of radioactive material used. For iridium 192 we do not exceed 150 mCi, and for cesium 137, 200 mCi for a treatment lasting 6 days.

2. Dosimetric Planning

Dosimetric planning consists of determining, before the application and in consideration of the dimensions of the target volume, the best radioactive setup in order to assure an optimal dose distribution in the treated volume.

To accomplish this goal, with the aid of computers we have been able to establish fundamental relationships between the treated volume and the radioactive material for different applications.

Single Plane Applications

The three dimensions of the treated volume are:

Length (L) of the treated volume (a). This is the distance between the boundaries of the treated volume on an axis parallel and equidistant to the two lateral most radioactive sources that establish the lateral corridors (b).

Thickness (T) of the treated volume. It is the distance between the boundaries of the treatment volume on an axis equidistant to the two radioactive sources delineating the lateral "corridors," and perpendicular to the center of the radioactive sources.

Width (W) of the treated volume. It is the distance between the boundaries of the treated volume on the axis perpendicular to the center of the radioactive sources and in the plane of these radioactive sources (c) (figure 1).

(a) In the case of a single radioactive line, the length is in the axis of the radioactive line itself. A specific definition of the "useful" length has been established in relation to the width (see "Studies for One Line" below).

(b) The term "corridor" corresponds to the space between two parallel radioactive lines:

In a setup of 2 lines, there is only 1 central corridor.

In a setup of 3 lines, there are 2 lateral corridors.

In a setup of 4 lines (figure 8), there are 1 central and 2 lateral corridors.

In a setup of 5 lines, there are 2 central and 2 lateral corridors.

In a setup of 6 lines, there are 1 central, 2 intermediate, and 2 lateral corridors.

(c) One could also define a segment of the width common to all radioactive setups in one plane: the "lateral margin" equals that fraction of the width between one of two lateral most radioactive lines, and the reference isodose (figure 8).

Dosimetric studies for 2 radioactive lines

Relationship between treated volume and radioactive material: the dimensions of the treated volume maintain a simple relation with the geometric factors of the radioactive material. Its length depends on the length of the radioactive material, its width and thickness depend on their spacing.

For the relationship between the length of the treated volume and the radioactive material, see table 1. (The ratios increase slightly when the radioactive lengths change from 1 to 10 cm: .65 to .75 for D. R. 85% D. B., and .88 to .94 for D. R. 70% D. B.) The length is practically independent of the spacing.

The relationship between the width of the treated volume and the radioactive material is also shown in table 1. The width is practically independent of the radioactive length for the same spacing.

The relationship between the thickness of the treated volume and the radioactive material may be seen in table 1. (These ratios become slightly larger when the radioactive lengths vary from one to 10 cm: .46 to .59 for D. R. 85 percent D. B. and .77 to .92 for D. R. 70 percent D. B.)

TABLE 1

		D.R. 85%	D.R. 70%
$\frac{\text{Length of treated volume}}{\text{Radioactive length}}$	=	0.70	0.90
$\frac{\text{Width of treated volume}}{\text{Spacing}}$	=	1.75	1.90
$\frac{\text{Lateral margin}}{\text{Spacing}}$	=	0.37	0.45
$\frac{\text{Thickness of treated volume}}{\text{Spacing}}$	=	0.50	0.85

Relationship of Width and Thickness in the treated volume:		D.R. 85%	D.R. 70%
$\frac{\text{Width}}{\text{Thickness}}$	=	3.5	2.3

(These percentages vary moderately when the radioactive lengths vary from 1 to 10 cm: 3.9 to 3 for D. R. 85 percent D. B. and 2.5 to 2.1 for D. R. 70 percent D. B.)

Relationship of Length and Width in the treated volume:

For small radioactive lengths, the width is numerically larger than the length. For larger radioactive lengths, the length is numerically larger than the width. There exists a zone of transition where the lengths and the widths are equal (see table 2).

TABLE 2

Radioactive lengths so that lengths and widths of treated volume are equal (cm)	Spacing (cm) D.R. 85%	 D.R. 70%
2.5	1.5	1.3
3.0	1.8	1.6
3.5		1.9

Thickness and diameter of the overdosage isodose:

In the case of a uniform reference dose, the thickness of the treated volume grows by a factor of 2.3 when the radioactive length varies between 1 and 10 cm, while the diameter of the overdosage isodose (2 D.R.) in the same conditions grows only by a factor of 1.3 (figure 9). In clinical applications with two active lines, if one compares the smallest treated volume (radioactive length, 1 cm; spacing, 0.8 cm, D.R. 85 percent D.B.) and the largest treated volume (radioactive length, 10 cm; spacing, 2.2 cm, D.R. 70 percent D.B.), the following figures are obtained for the thickness of the treated volume and the diameter of the overdosage isodose:

	Thickness	2 D. R. (in cm)
Minimal volume	0.36	0.35
Maximal volume	1.8	0.97

Dosimetric studies for 1 line

With a single radioactive line, the basic dose no longer is recognizable. The relationship between the radioactive setup and the treated volume is therefore established only by analogy with those already discussed for 2 radioactive lines. Only 2 dimensions are left to study in the treated volume:

The width, which is identical to the thickness;

The length, situated in the axis of the radioactive line.

1. Width of the treated volume

Only the maximum width is defined in relation to the radioactive length. By analogy with the dosimetric distribution for two radioactive lines, and based on the maximum dimensions accepted for the area of overdosage (less than 1 cm), we propose a maximum width corresponding to a reference dose of 70 percent for two radioactive lines. For the same radioactive length and the usual maximum spacing, see table 3. (Figures 10, 11.)

In relation to the radioactive length, the values are shown in table 3.

TABLE 3

Radioactive Length (in cm)	Width of Treated Volume (in cm)
1	0.9
2	1.2
3	1.3
4	1.4
5	1.4
6	1.5
7	1.5
8	1.5
9	1.6
10	1.6

2. Length of the Treated Volume

Situated in the axis of the radioactive line, the length of the treated volume projects beyond the boundaries of the radioactive length. It is, however, necessary to define a "useful length" so that at each extremity the width of the treated volume is equal to 90 percent of the width calculated at the center of the radioactive line. A computer study of the position of the "90 percent width" (W 90) in relation to the length of the radioactive line gives the following relation for radioactive lines of one to 10 cm (figure 12):

$$\frac{\text{"Useful" length}}{\text{Radioactive length}} = .7$$

Dosimetric studies of 3, 4, and 5 lines

For 3 lines, the definitions remain identical to those for 2 lines. The basic dose is calculated for 2 points symmetrically located on both sides of the central radioactive lines.

For 4 and 5 lines, we have established the basic dose at points equidistant from the 2 most lateral lines. The relationships between treated volume and radioactive material that we established for 2 radioactive lines can, therefore, be transposed with minimal variations (figures 13, 14).

In the case of 5 radioactive lines, the following is to be noted:

1. The basic dose calculated in the "lateral corridors" is 4 to 8 percent less than that calculated at equidistant points in the central corridors.

2. The relation $\frac{\text{length of treated volume}}{\text{radioactive length}}$ is practically identical to that for 2 lines:

D.R. 85% D.R. 70%

$$\frac{\text{length of treated volume}}{\text{radioactive length}} = \quad .7 \qquad .9$$

3. The relation $\frac{\text{lateral margin}}{\text{spacing}}$ is slightly less than for 2 lines:

$$\frac{\text{lateral margin}}{\text{spacing}} = \quad \overset{.34}{(\text{against } .37)} \quad \overset{.40}{(\text{against } .45)}$$

4. The relation $\frac{\text{thickness}}{\text{spacing}}$ is slightly larger than for 2 lines:

$$\frac{\text{thickness}}{\text{spacing}} = \quad .6 \qquad .95$$

(against .5)(against .85)

These percentages have been calculated in the lateral corridors. In the central corridors, they should be augmented by 8 to 10 percent for the length of the treated volume, and about 25 percent for the thickness.

Several Planes Applications

The study of radioactive setups in 2 or 3 planes made up of straight and parallel lines confirms the validity of the relationship between treated volume and radioactive material. The calculated dose at equidistant points in the central corridors can increase by as much as 10 to 15 percent compared with the basic dose in the lateral corridors. This increase, a result of the concept of two target volumes, is biologically acceptable and an additional guarantee in regard to the central zone of the target volume, where the least vascularized and less radiosensitive part of the tumor is located.

Conclusion

According to the principles of our relational system, the spacing between radioactive lines is greater as the lines become longer. Three reasons justify this statement:

1. Physical: The diameter of the isodose surrounding a radioactive line grows proportionally as the distance between the radioactive source and the isodose in question becomes greater.

2. Technical: In view of the difficulty of assuring strict parallelism for the longer lines, the risk of creating cold or hot spots becomes greater with very small spacing.

3. Clinical: The thickness is usually greater for longer target volume.

We have, however, established an upper limit of 2.2 cm for spacing, corresponding to one diameter of the overdosage isodose of approximately 1 cm for radioactive lines of 10 cm with a D. R. of 75 percent D. B. (exactly .97 cm). In view of actual clinical experience, we do not advise exceeding this diameter; it seems, in fact, that the healing of the tissues is difficult in areas exceeding 15,000 rads (with risk of necrosis), and with a diameter exceeding 1 cm.

Radioactive lengths of between 1 and 10 cm often are used in clinical situations. It is possible to foresee applications with longer radioactive lengths, without increasing the maximum spacing of 2.2 cm.

In consideration of the dose output, and in view of the duration of the application, it is important to appreciate the relationship between the basic dose and the spacing of the radioactive lines of different lengths (see table 4). A provisional atlas of different radioactive setups with straight and parallel lines is now under study (figure 15).

Special Considerations

1. Cylindrical Volumes (straight and parallel radioactive lines). On a single circumference, we recommend not more than 5 radioactive lines in the form of a pentagon, seen on a transverse plane. With the maximum spacing of 2.2 cm between each line, one establishes a treated volume that resembles a cylinder, with a diameter of 4 cm within the minimum boundaries of the reference isodose of 85 percent (figure 16).

When the diameter exceeds 4 cm, it is necessary to add supplemental lines on the circumference and a central radioactive setup. In view of the increasing treated volume, this setup consists of 1, 3, or 5 central lines.

TABLE 4

Radioactive length (in cm)	Spacing between two parallel lines (in cm)			
1	0.8	0.9	1.0	1.1
2	1.1	1.2	1.3	1.4
3	1.2	1.3	1.4	1.6
4	1.2	1.3	1.5	1.7
5	1.3	1.4	1.6	1.8
6	1.3	1.4	1.6	1.9
7	1.3	1.5	1.7	1.9
8	1.3	1.5	1.7	2.0
9	1.3	1.5	1.7	2.0
10	1.3	1.5	1.8	2.1
	40	35	30	25

D. B. in rads/hour

(iridium 192. linear activity: 1 mCi/cm)

2. Curved volume (curved and parallel lines). The dose distribution is asymmetrical, being higher on the concave side. For an arc less than 30 degrees, one can practically neglect the curvature in the area less than 1 cm from the radioactive lines. For an arc greater than 30 degrees, the dose should be corrected with the help of tables, such as those of Meredith. One can also transpose small linear segments to the curved lines corresponding with a line joining arcs of 30 to 45 degrees. In fact, a better solution is offered by the computer.

3. Volume in the Form of Buckles. In the case of buckle implantations, conditions are similar to those in the use of radioactive pins. In view of slight biological differences, the dose can be calculated as if one were dealing with a straight radioactive line passing transversely through the peak of the buckle. Once again, however, the computer offers a better solution.

4. Volume in the Form of Triangles. One is called on in certain cases to encompass a lesion with three radioactive lines forming a triangle (equilateral as much as possible). In order not to exceed the overdosage margin, the sides of the triangle should be less than 4 cm. The points of intersection will be left inactive, in order to avoid hot spots. The basic dose can be calculated at the center of the setup with the use of standard isodoses. However, a detailed calculation of the dose cannot be established (especially in regard to the reference isodose) except with the use of computer (figure 17).

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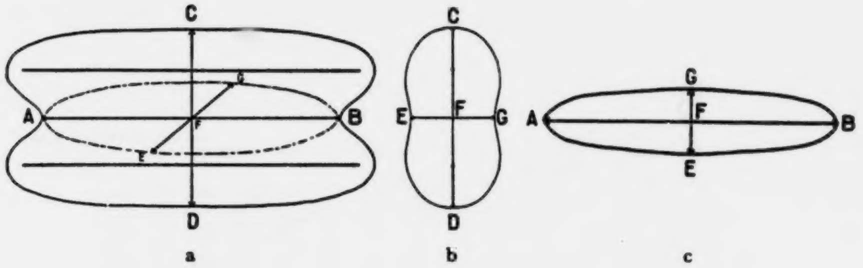


Figure 1. Dimensions of the treatment volume, the figure being to scale for the 70 percent isodose around 6 cm long sources separated by 1.68 cm. (a) Composite view showing the three dimensions: length (AB), width (CD), thickness (EG), all taken through the central point (F), the position of the basal dose. (b) and (c) show the two planes perpendicular to ABCD.

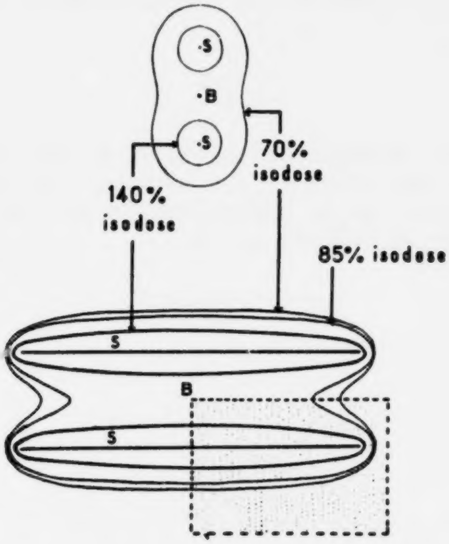
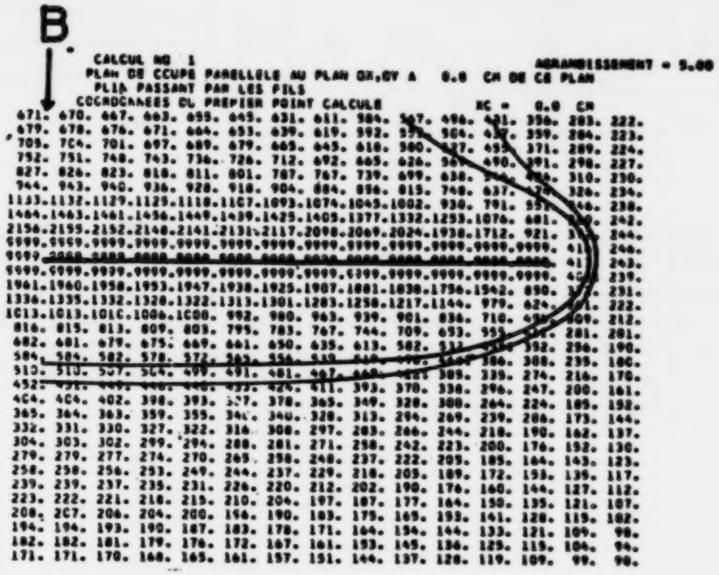


Figure 2. Reconstruction of the complete plane (cf. figure 1). The 140 percent isodose encloses the 'high dose zone' corresponding to a reference isodose of 70 percent. The example taken is for 6 cm sources, separated by 1.68 cm. The basal dose (B) is 671 rad per 24 hours.



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CALCUL NO  1                                                    AGRANDISSEMENT = 5.00
PLAN DE COUPE PARALLELE AU PLAN OX,OY A   0.0  CM DE CE PLAN
PLIA PASSANT PAR LES FILS
COORDONNEES DU PREMIER POINT CALCULE                    XC =   0.0  CM
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Figure 3. Example of calculation page showing the isodoses in the plane of the sources. As the isodoses are symmetrical, it is sufficient to calculate that portion of the plane that is shown.

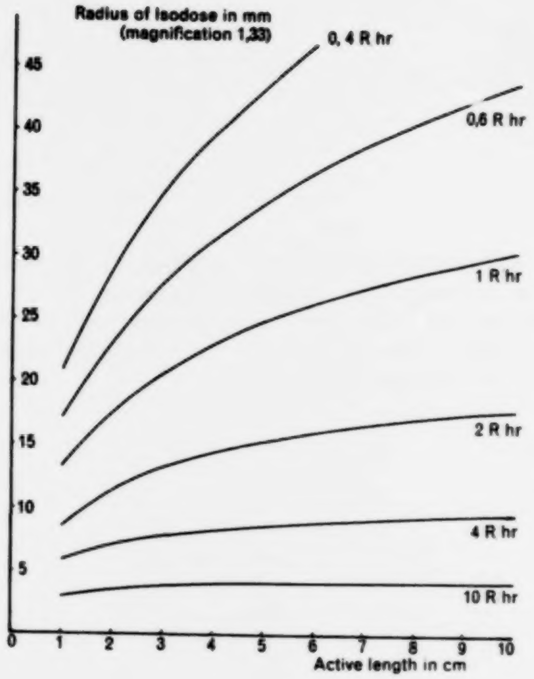


Figure 4. Variation of radius of isodose circle with active length of source. Calibration graphs representing the increase in diameter of standard circular isodose distributions as a function of radioactive lengths [the increase in diameter of the isodoses is noted to be small a short distance from the active wire (isodose 10) and rises progressively as the distance from the source is increased (isodoses 2-1-0-6-0-4). This explains why the radioactive linear sources can be spaced more widely apart, as their length increases without dangerously augmenting the cuff of proximal overdosage.]

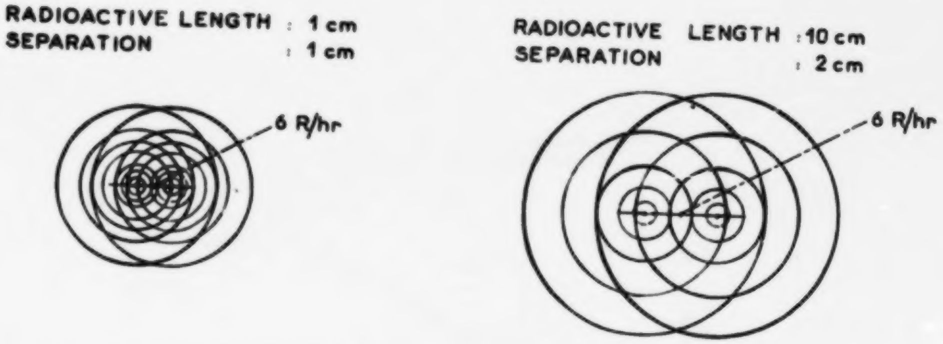

RADIOACTIVE LENGTH : 1 cm
SEPARATION : 1 cm
6 R/hr
RADIOACTIVE LENGTH : 10 cm
SEPARATION : 2 cm
6 R/hr

Figure 5. Universal circular isodose curves, 1 R/hour for 1 mCi/cm. Comparison between spacing two radioactive sources of 1 cm length in a small target volume and two radioactive sources of 10 cm length in a large target volume. The values of the standard circular isodoses are 10, 4, 2, 1, 0.6, (0.4), R/h.

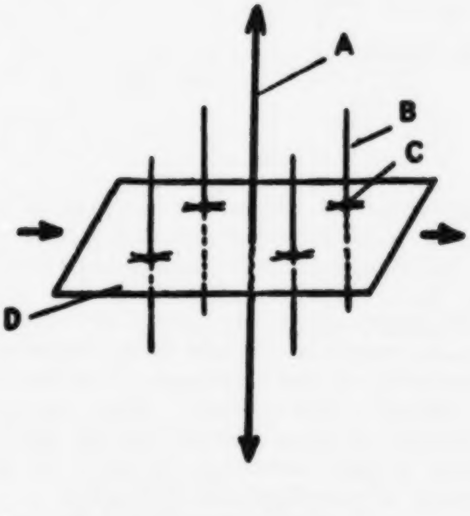


Figure 6. Technique of dosimetry around points: (A) Axis of implantation; (B) Radioactive line; (C) Point; (D) Plane at right angles to the axis of implantation.

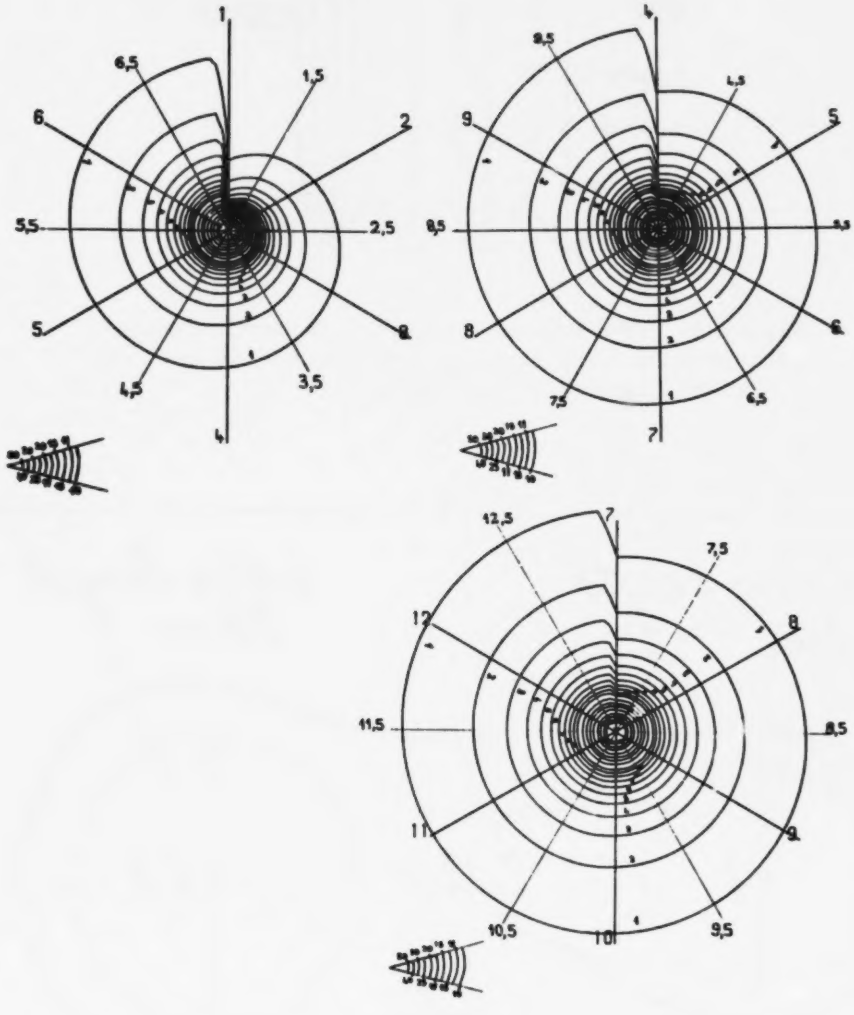

1
6,5
1,5
6
2
5,5
2,5
5
3
4,5
3,5
4
4
9,5
4,5
9
5
8,5
5,5
8
6
7,5
6,5
7
7
12,5
7,5
12
8
11,5
8,5
11
9
10,5
10
9,5

Figure 7. The three isodose "snail" curves calculated on the computer and drawn on transparent paper. The values of the nearest isodose are identified on a scale below and at the left of each "snail."

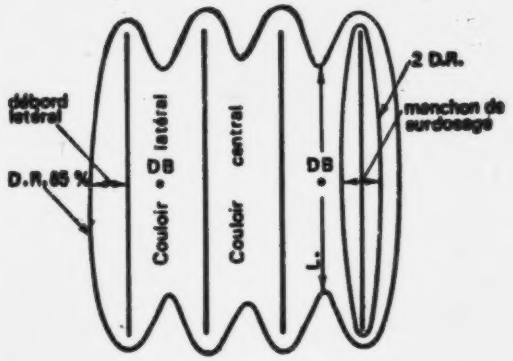

2 D.R.
débord latéral
manchon de surdosage
D.R. 85 %
DB
DB
Couloir latéral
Couloir central
L

Figure 8. Provisional dosimetry in brachytherapy. Distribution of 4 parallel radioactive lines 6 cm in length, spaced 1.5 cm apart.

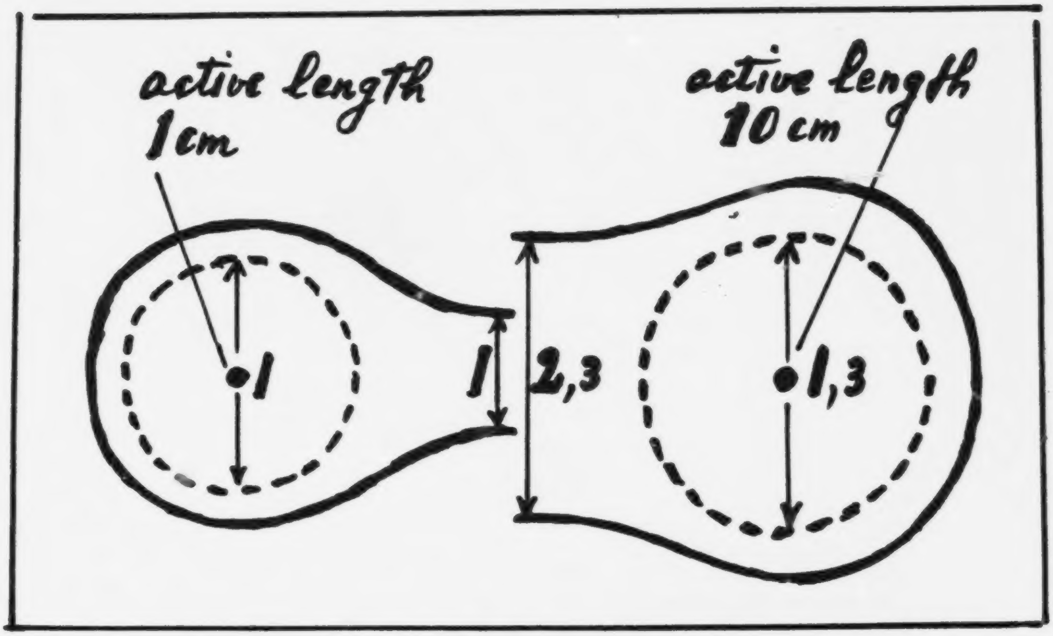
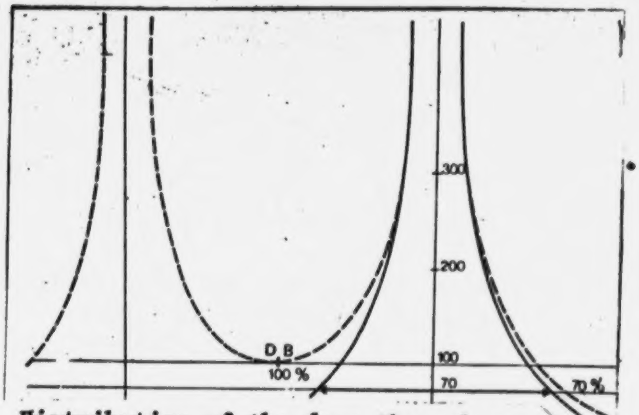

active length 1cm
active length 10 cm
1
1
2,3
1,3

Figure 9. The diameter of the treated volume increases with the length of the source.



Distribution of the dose through a plane passing through the center:

- - - - *from 2 radioactive lines 6 cm long, with 1.9 cm separation*

——— *from 1 radioactive line 6 cm long*

Figure 10. Maximum width corresponding to a reference dose of 70 percent for 20 radioactive lines.

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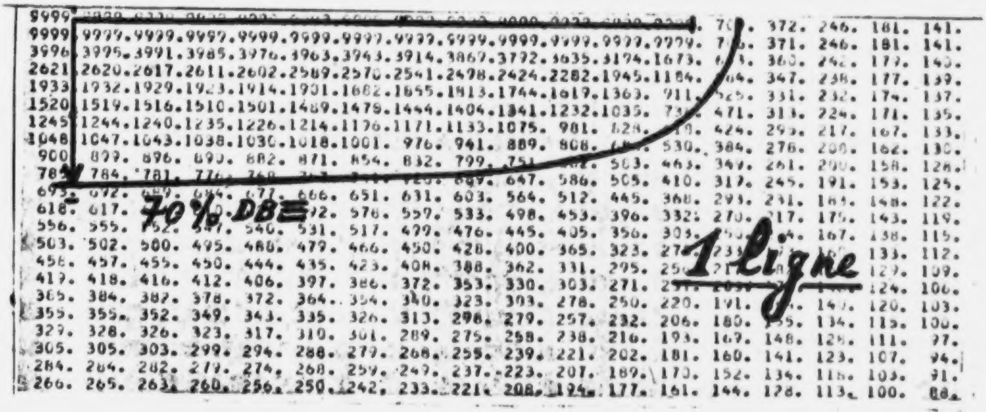

9999.	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	372.	246.	181.	141.
9999.	9999.	9999.	9999.	9999.	9999.	9999.	9999.	9999.	9999.	9999.	9999.	9999.	[illegible]	371.	246.	181.	141.
3996.	3995.	3991.	3985.	3976.	3963.	3943.	3914.	3867.	3772.	3635.	3174.	1673.	[illegible]	360.	242.	177.	140.
2621.	2620.	2617.	2611.	2602.	2589.	2570.	2541.	2498.	2424.	2282.	1945.	1184.	[illegible]	347.	238.	177.	139.
1933.	1932.	1929.	1923.	1914.	1901.	1882.	1855.	1813.	1744.	1619.	1363.	911.	[illegible]	331.	232.	174.	137.
1520.	1519.	1516.	1510.	1501.	1489.	1479.	1444.	1404.	1341.	1232.	1035.	[illegible]	471.	313.	224.	171.	135.
1245.	1244.	1240.	1235.	1226.	1214.	1196.	1171.	1133.	1075.	981.	628.	[illegible]	424.	293.	217.	167.	133.
1048.	1047.	1043.	1038.	1030.	1018.	1001.	976.	941.	889.	808.	[illegible]	530.	384.	276.	208.	162.	130.
900.	899.	896.	890.	882.	871.	854.	832.	799.	751.	[illegible]	563.	463.	349.	261.	200.	158.	128.
785.	784.	781.	776.	768.	[illegible]	[illegible]	[illegible]	[illegible]	647.	586.	505.	410.	317.	245.	191.	153.	125.
693.	692.	689.	684.	677.	666.	651.	631.	603.	564.	512.	445.	368.	293.	231.	[illegible]	148.	122.
618.	617.	[illegible]	[illegible]	[illegible]	[illegible]	578.	559.	533.	498.	453.	396.	332.	270.	217.	175.	143.	119.
556.	555.	552.	547.	540.	531.	517.	499.	476.	445.	405.	356.	303.	[illegible]	[illegible]	167.	138.	115.
503.	502.	500.	495.	488.	479.	466.	450.	428.	400.	365.	323.	[illegible]	[illegible]	[illegible]	[illegible]	133.	112.
458.	457.	455.	450.	444.	435.	423.	408.	388.	362.	331.	295.	[illegible]	[illegible]	[illegible]	[illegible]	129.	109.
419.	418.	416.	412.	406.	397.	386.	372.	353.	330.	303.	271.	[illegible]	[illegible]	[illegible]	[illegible]	124.	106.
385.	384.	382.	378.	372.	364.	354.	340.	323.	303.	278.	250.	220.	191.	[illegible]	147.	120.	103.
355.	355.	352.	349.	343.	335.	326.	313.	298.	279.	257.	232.	206.	180.	[illegible]	134.	115.	100.
329.	328.	326.	323.	317.	310.	301.	289.	275.	258.	238.	216.	193.	167.	148.	128.	111.	97.
305.	305.	303.	299.	294.	288.	279.	268.	255.	239.	221.	202.	181.	160.	141.	123.	107.	94.
284.	284.	282.	279.	274.	268.	259.	249.	237.	223.	207.	189.	170.	152.	134.	116.	103.	91.
266.	265.	263.	260.	256.	250.	242.	233.	221.	208.	194.	177.	161.	144.	128.	113.	100.	88.

70% DB=

1 ligne

Figure 11. Study around a single iridium 192 wire 6 cm in length. The reference isodoses correspond to the 70 percent isodose around 2 parallel sources of same length and spacing.

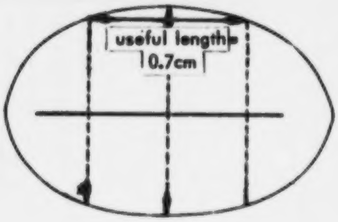

Figure 12. Study for one line. Wire of one cm of radioactive length, definition of the useful length.

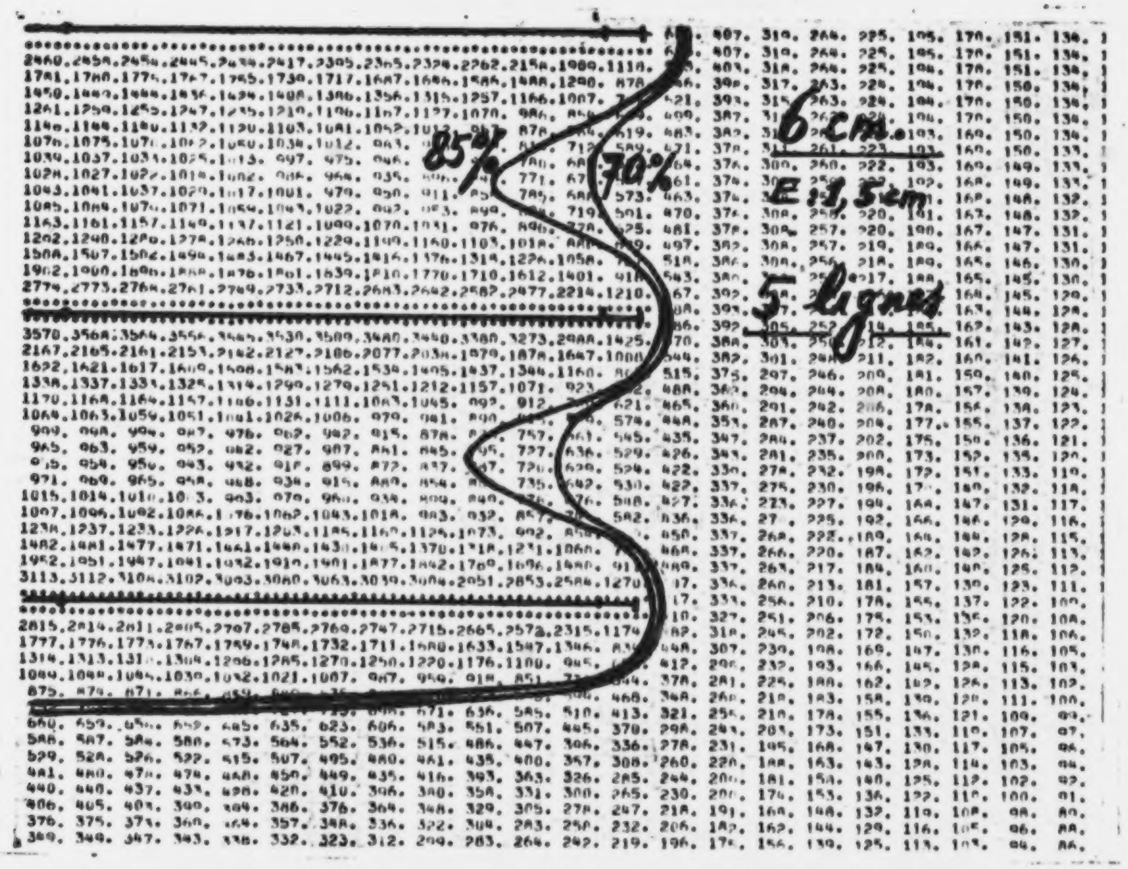

Figure 13. Dosimetry in the plane of 5 parallel radioactive lines, 6 cm long and spaced 1.5 cm apart.

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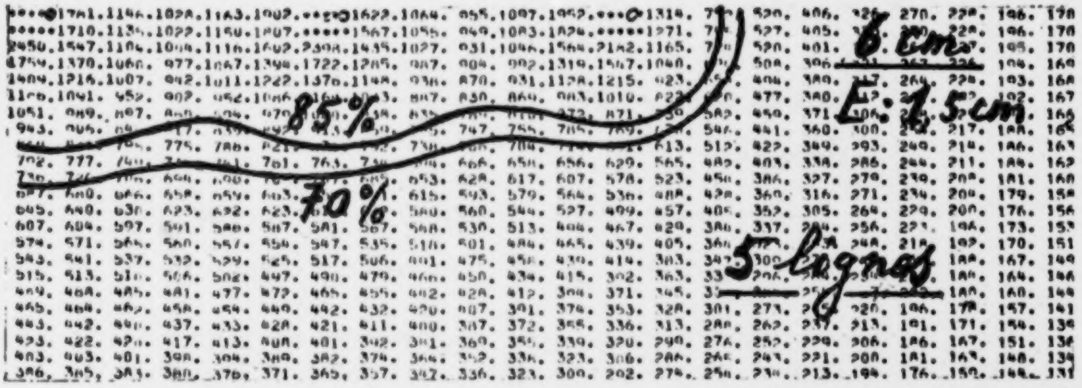
6 cm
E: 1.5 cm
85%
70%
5 lignes

Figure 14. Study around 5 parallel radioactive lines 6 cm in length, spaced 1.5 cm apart. Dosimetry in the perpendicular plane of the wires and passing through their center.

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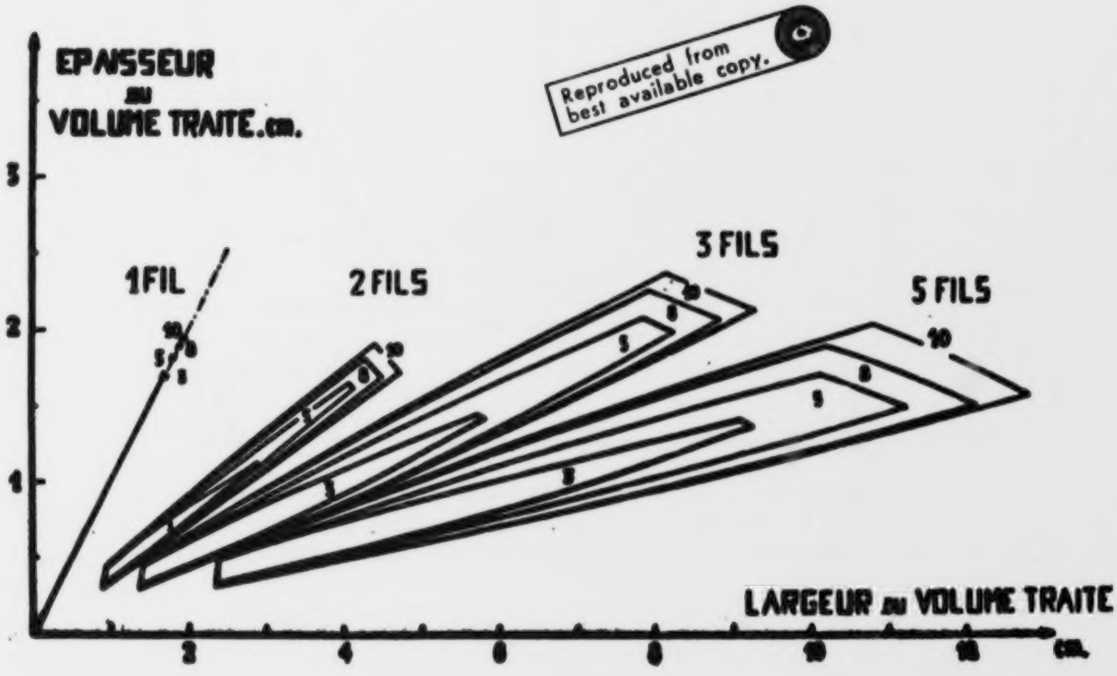

Figure 15. Provisional atlas of different radioactive setups with straight and parallel lines.

DOSE DE BASE = 100

ISODOSES:

———————— 200 120 85 50

—·—·—·— 150 100 70

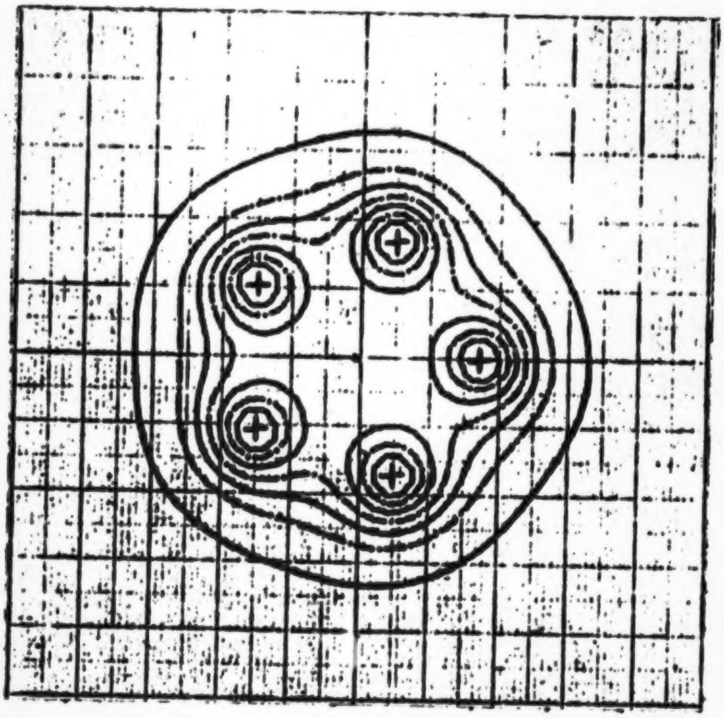

Figure 16. On a single circumference, not more than 5 radioactive lines in the form of a pentagon, on a transverse plane, are recommended.

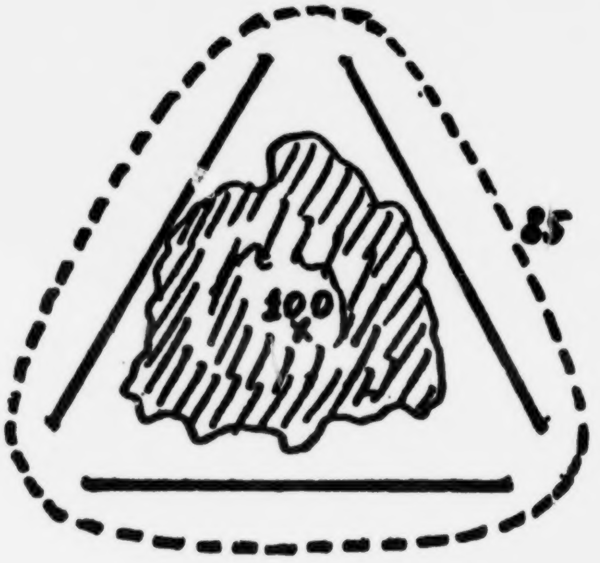

Figure 17. In order not to exceed overdosage at meeting point of sources, sides of a triangle should not exceed 4 cm.

CANCER OF THE CERVIX

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CONSIDERATION OF DOSE RATE
IN INTRACAVITARY RADIATION THERAPY SYSTEMS[a]

H. D. Suit, M.D., Ph.D., Barry Brown, Ph.D.,
H. R. Withers, M.D. and James Thompson, Ph.D.

The introduction of remote control "afterloading" devices into clinical medicine presents a unique opportunity to investigate the role of dose rate as distinct from dose distribution pattern.

One of the great traditions in radiation therapy has been that optimal results are obtained by interstitial, intracavitary, or surface mold techniques. There are several important differences in the physical characteristics between such techniques and the standard fractionated dose radiation therapy. These include dose distribution pattern, total time, and dose rate. For interstitial and intracavitary therapy, clinically effective dose levels are administered in a nonhomogeneous pattern to a relatively small volume, while external beam techniques feature a rather homogeneous distribution throughout a comparatively large volume. For surface mold treatments, the dose distribution is not dissimilar to that which may be achieved with external beam techniques.

With respect to total time, interstitial and mold therapy have been based on a single procedure that extends over some 6-10 days; intracavitary therapy usually features one to several insertions over 2-3 weeks. In contrast, external beam therapy is designed for 18-40 dose fractions over 4-8 weeks.

As to dose rate, interstitial or intracavitary procedures utilize average dose rates in the treatment volume of 40-60 rad/hr, whereas each dose fraction with external beam therapy is given at dose rates of 3,000-24,000 rad/hr (50-400 rad/min). Various groups are now employing the remote control afterloading devices for intracavitary and surface mold treatment procedures, and very high dose rates have now proven feasible from a radiation protection point of view.

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[a] This paper is supported in part by the United States Public Health Service grants CA05047, CA6294, CA11138 and CA11430.

Accordingly, for a fixed dose distribution pattern the effect of marked variation in dose rate can be investigated. If the clinical impressions of our teachers have been correct (that better results are achieved using low dose rates), this should be documented; it might have applications for external beam therapy. Pierquin, of the Institute Gustav-Roussy, recently has started a study of low dose rate external beam therapy.

The question of the relative importance of dose distribution and dose rate, a basic one in radiation therapy, has received very little attention from either clinical or laboratory investigators. At this time, considerable effort is being put into planning a project to compare the clinical usefulness of negative pi mesons relative to a good fast neutron beam (viz, produced by a high energy cyclotron). The principal advantage claimed for pi mesons is a clear superiority in dose distribution patterns. Perhaps some evaluation of the role of dose distribution could come from appropriate clinical trials utilizing widely different dose rates in the treatment of patients by the remote control afterloading equipment. If the same clinical result were achieved with low dose rate (for example, standard radium loading) and high dose rate fractionated treatment as employed by Joslin et al. (1, 2) for the treatment of carcinoma of the uterine cervix (intracavitary) and various superficial lesions (surface mold techniques) there would be significant evidence that the dose rate *per se* is not an important factor in the therapeutic ratio, and that dose distribution may be.

In this presentation, we will consider some of the uncertainties in utilization of the formula developed by Liversage, which provides an empiric method for estimating the number of equal dose fractions (high dose rate) into which a total dose D should be divided so as to produce the same degree of damage as if D were given continuously over a total time t.

The dependence of the response of a cell population on the dose rate-dose fractionation schedule is a complex function of a vast array of independent and dependent variables, each of them important. (These are listed in table 1.) As is obvious with such a richness of variables, tissue models that incorporate all these parameters can be made to perform according to the wishes, biases, or expectations of the model builder. This is especially true when attempts are made to predict the response of human tissue, as the appropriate values of these parameters for the critical cell population are largely unknown. An important fact is that there is no certainty which normal tissue is critical or dose limiting. Also, the role of the hypoxic cell in determining the response of human tumor tissue to radiation is not established. As an additional comment, values for certain of these parameters probably change during the course of treatment.

As part of our program to investigate at the laboratory level the role of dose rate and fractionation number in determining the response of murine tumor and normal tissue to gamma irradiation, several model tissues have been formulated. The effect of variation of each of the parameters listed in table 1 on the response to continuous and fractionated irradiation is being assessed. In simple terms, the properties of the model are:

(1) Cell death is described as a multi-target, single hit process which stipulates that the cell dies only if all of the n targets are inactivated at any one time.

(2) A specified proportion, ω, of the absorbed energy produces damage that is non-repairable. Cell killing as a result of these events follows single-hit, single target kinetics. These processes are viewed as producing either a class of damage for which the cell does not have an effective repair system or non-repairable damage due to high LET events that occur at ends of delta ray tracks, etc. Therefore $1-\omega$ is the proportion of energy that produces damage which may be repaired. This is true for any cell, provided $\leq$ n-1 targets are hit.

(3) Damage in the repairable category is repaired at a rate corresponding to the repair half-time. For our purposes, RT is defined as the half-time for repair of a single target.

(4) As we do not have appropriate data regarding the age response function in human tissue, our calculations to date have been based on a conveniently simple model in which 10 percent of cells are in a sensitive phase (n=1), and 90 percent are in a resistant phase (n=2-10 and ω=0.0-0.30). The actual situation is, of course, more complex; radiosensitivity (D_0 and n) is known to vary with cell age, and the cell cycle phase distribution is perturbed by irradiation. In addition to D_0 and n, values for other parameters probably are dependent on the position of the cell in the cell cycle: for example, RT, ω, and sensitivity to blockage of progress through the cycle.

(5) The cell proliferation factor is designated q: the fractional increase in number of viable cells per traversal of the cell cycle. In non-growing normal tissues, q is 1.0; for tumors, q may range from 1.0 to 2.0. A realistic value for q in human tumor cell populations is probably in the range of 1.0 to 1.20, with 1.05 - 1.10 being a reasonable figure. It is much less than 2.0 because of the high cell loss factor (3).

(6) Transfer of cells from hypoxic status to aerobic status has not been considered in our current calculation. A detailed consideration of these analyses will be presented in a separate paper.

At this point, we turn to a formula developed by Liversage (4) which gives the number of fractions (ν) in which a total dose (D) should be delivered to elicit the same response as if D were delivered continuously over a time (t). This number of fractions (ν) will be influenced to some degree by all of the factors we have mentioned, and we are conducting modeling to determine the range of conditions in which the formula is a reasonable approximation. We note that Elkind (5) has some criticisms of the methodogy leading to this formula. Nonetheless, the formula is appealing because of its simplicity, and it is now being used to some extent by clinicians. The Liversage formula is:

$$\nu = \frac{ut}{2\left[1 - \frac{1}{ut}\left(1-e^{-ut}\right)\right]}$$

Where t is the known duration of the continuous irradiation, and u is 0.693/τ, τ is a measure of the repair half-time as defined by Oliver (6). (Oliver's definition is complex and will not be given here; it is based upon analysis of the cell survival curve -- single dose, high dose rate -- and the split dose recovery curve.) Specifically, τ is not the same as the RT which we have employed (half-time for repair of a damaged target). Liversage proposes that a clinically useful value for ν may be calculated if a value is assigned to the single parameter τ. This means that if the same dose distribution pattern and number of mgm/hrs were employed, the result would be equivalent for continuous treatment or for ν fractions. For example, if t for an intracavitary therapy procedure is 144 hrs, and τ is given the reasonable value of 1.5 hours, then ν would be 34. Provided the τ value were correct, and applicable to cells of the critical normal tissue and the tumor tissue, the therapeutic ratio would be expected to be the same for the continuous and fractionated treatment regimens.

Two reasonable questions are: What would be the predicted effect of a small mistake estimating τ, and what would be the effect of a difference between τ (normal tissue) and τ (tumor tissue)?

Figure 1 demonstrates the relationship between ν and t for τ values of 0.5, 1.0, 1.5, 2.0, and 3.0. Obviously, the value selected for τ is highly important in determining the number of equal doses into which the total dose should be fractionated. This is considered in more detail in figure 2, which illustrates the dependence of ν on τ for the particular value for t of 144 hours. As mentioned earlier, where τ = 1.5 hours we find the proposed ν to be 34. If, however, we knew τ to be 1.5 ± 20 percent, then the correct ν would be in the range of 28 to 41.

There is much evidence from laboratory experiments to demonstrate that rates of repair of radiation damage vary considerably from one tissue system to another. For example, a crude estimate of repair half times may be made from the slope of the initial part of the split dose recovery curve. When this is done for the data from cells of mouse skin (7), jejunal crypt (8), and stomach mucosa (9), RT values are ∿1.5, 1.5, 0.5 hours. In our work with a mouse mammary carcinoma, the corresponding figure would be ∿1 hour (10). Studies on the Ehrlich ascites tumor cell line indicates a value ≥ 2 hour (11). Furthermore, repair half-time may vary throughout the division cycle, as is shown by interesting data from Whitmore et al. (12), using LP59 cells cultured in vitro (figure 3). They determined recovery curves for LP59 cells in G_1, early S, mid S, and late S phases of the cell replication cycle. First and second doses were 700 and 500 rads respectively. To reduce progression of cells during t_1 (time between doses), the cells were incubated at 25 degrees C. As indicated in the figure, repair rate for the LP59 cells appears appreciably slower for G_1 than for the S phase cells. These various data show that there is a spread in repair half-times of radiation damage. This is likely also to be the case for human tissue cells.

Accordingly, simple selection of a reasonable average value might well lead to an unfortunate choice of ν value. A further implication of variable repair half-times is the difference that may exist between normal and malignant tissue. Thus, if the actual values of τ were 2 for the tumor tissue and 10 for the normal tissue, but a treatment plan for continuous irradiation (τ = 144 hours) were modified for multiple fractions using a constant τ value of 1.5, the ν value used would of course be 34 as shown by figure 2. But ν should have been 25 and 50 for an equivalent effect on tumor and on normal tissues, respectively. The result would be that the tumor tissue is underdosed (a fixed total dose given in 34 instead of 25 fractions) and the normal tissue overdosed (a total dose given in 34 instead of 50 fractions) relative to what could be achieved with continuous exposure.

There is another aspect to these considerations. All the above calculations by Liversage, Oliver, and ourselves have been based on the convenient assumption that repair rate can be described by a simple exponential function. This may not be so in many instances: repair kinetics may be different for different classes of damage. For example, the recovery curve (figure 4) for stem cells of the mouse stomach by Chen and Withers (8) is composed of at least 2 components: an initial curve indicating a "half-time for repair" of ∿ 30 minutes, and a second and very much slower (quantitatively less important) curve with a slope of one-tenth the initial curve. This curve contrasts with that for jejunal crypt cells or basal cells of skin where aparently there is no initial rapid repair component, although over a range of t_1 of 1 to 4 hours there are many fewer points for the skin and intestinal crypt system.

In summary on this point, there is good evidence indicating widely different "repair half-times" for different mammalian cell systems. Furthermore, there may well be some dependence of repair rates on the position of the cell in the cell replication cycle, and in certain cell systems the initial portion of the recovery curve may be complex.

As a final caution on the use of a fixed repair half time, it should be noted that the repair half time as defined by Oliver and used by Liversage depends heavily on the target number, n. This is clear because computation of D_E depends heavily on the acute dose survival curve. Also, it is sensitive to the value for ω, q, and proportion of sensitive cells. This will be considered in detail in a separate report.

Here we present one figure from our initial results with this model. Figure 5 demonstrates the relationship between dose required to produce a survival fraction of 10^{-5}, and extrapolation number for both a fractionated and continuous course of radiation. As can be seen, the ratio of total dose for an equal effect from continuous or fractionated irradiation varies with n value in the range of 2 to 8, and the total dose or number of fractions (each fraction is set at 1.33 X D_0) for fractionated irradiation.

From the considerations presented here, there clearly is great uncertainty in selecting the appropriate values for the parameters to be used in estimating for fractionated irradiation a dose that is equivalent biologically to the dose conventionally given by continuous irradiation. The attempt to do so is not exciting, as there is no predicted benefit to the patient, but only an expected reduction in radiation exposure levels to medical and para-medical personnel.

SUMMARY

General comments have been made regarding the opportunities to test the role of dose rate, as distinct from dose distribution, available now that remote control afterloading devices are being employed with high dose rate techniques. Discussion was presented regarding the differences between various mammalian cell lines as to rates of repair of radiation damage, and the effect these differences would have on the calculated number of fractions into which the same total dose should be divided in order to achieve the same biological effect. This simply emphasized that calculation of the relationship between continuous and fractionated irradiation is uncertain. Because of the number and complexity of relevant variables,

one cannot confidently predict with required accuracy the total dose and number of fractions that should be employed in high dose rate intracavitary technique to elicit the same tissue response as standard low dose rate intracavitary techniques.

A highly relevant question is whether the potential gain is worth the risk. Are there other techniques for reducing nursing personnel exposure dose that do not require a major shift in dose rate employed? This is a reasonable question since there is no proposal of benefit to the patient by utilizing the very high dose rates with intracavitary technique.

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TABLE 1. FACTORS THAT DETERMINE THE RESPONSE OF CELLS TO CONTINUOUS IRRADIATION

1. D_o, n, Single dose, high dose rate irradiation
    a. Age response function; duration of various phases of cell cycle
    b. Proportion of damage that is not repairable (ω)
    c. RT repair half time (simple exponential or complex function indicating multiple processes)
    d. Sensitivity of cell progression
2. Proliferative activity
    a. T_c median cell cycle time
    b. Fractional increase in clonogenic cell number per median cycle time (q)
3. Changes in tissue oxygenation

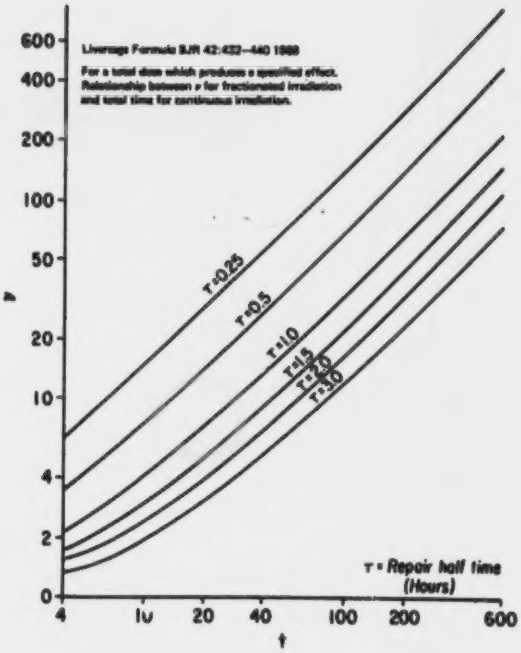


Figure 1. Relationship between ν and t for various values of τ, using the Liversage formula (3).

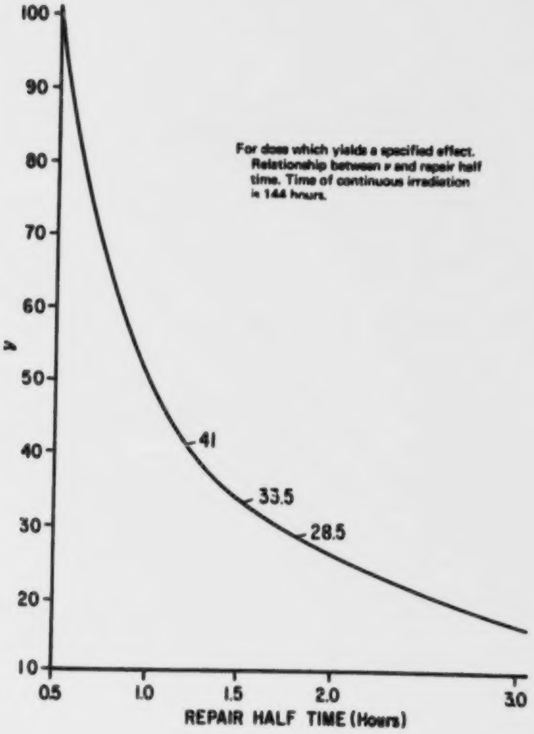


Figure 2. Relationship between ν and τ for the total treatment time in continuous irradiation of 144 hours

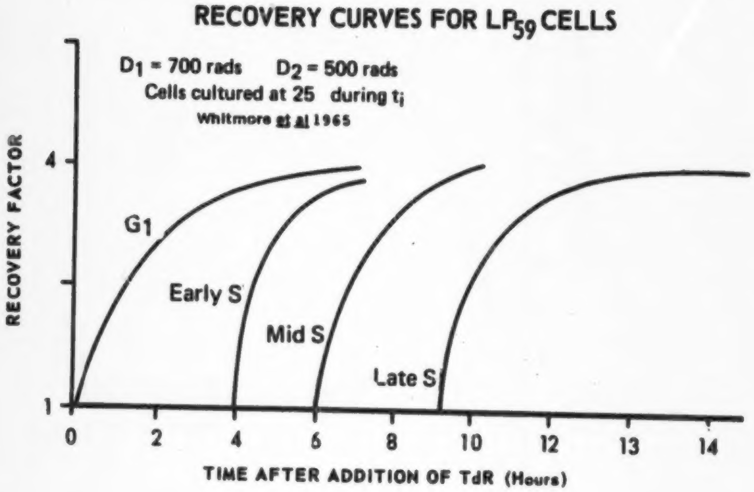
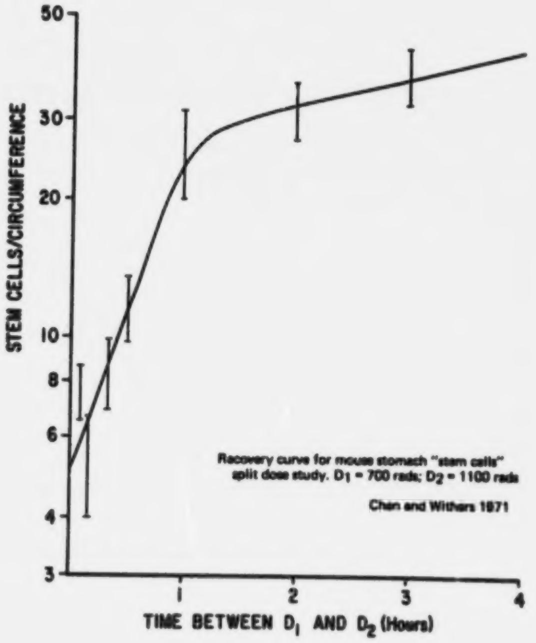


Figure 3. Recovery curve for LP59 cells where 1st dose = 700 rads, and 2nd dose = 500 rads (11).



Recovery curve for mouse stomach "stem cells" split dose study. D_1 = 700 rads; D_2 = 1100 rads

Chen and Withers 1971

Figure 4. Recover curve for "Stem Cells" of the C3H/Bu mouse stomach.

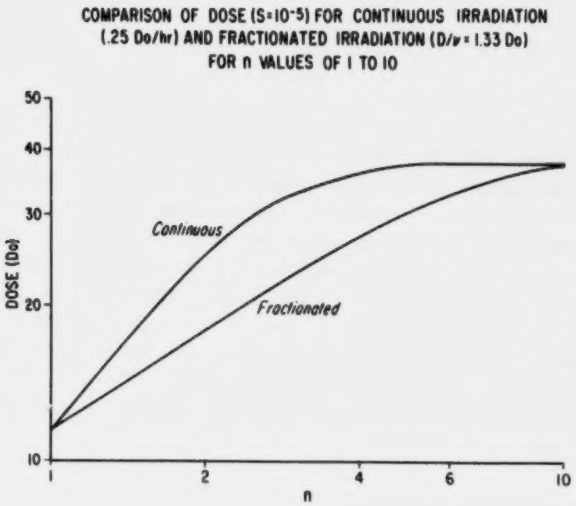


Figure 5. Dependence of dose which yields a surviving fraction = 10^{-5} for continuous irradiation (0.25 D_o/hour) and fractionated irradiation (1.33 D_o/fraction). See Text for details of the model.

CESIUM 137 AFTERLOADING SYSTEM FOR THE TREATMENT OF CARCINOMA OF THE CERVIX

Harry Horwitz, M.D.

The author's initial and principal motivation in designing an afterloading system (circa 1960) was to cut down on work, expense, fuss, bother, and mess. Cutting down on radiation exposure was an incidental consideration. Indeed, improving efficiency had more appeal at that time than cutting down on millirads received, and thus the system ultimately devised emphasized simplicity and ease in everyday use. In addition, the author had developed a revulsion to radium rooms because of "exposure" at a tender age to a couple of particularly unpleasant and unattractive radium rooms that never looked clean, nor had that bright, crisp, clinical, stainless-steel-and-ceramic-tile, uncluttered appearance which to a naive imagination seemed appropriate.

Radium tools were primitive; radiation protection was a matter of dexterity and speed; sterilization arrangements always seemed inadequate and unsatisfactory, with no clear concept as to how really to clean and sterilize radium within or without the different kinds of applicators. It was (and probably still is) difficult to get help in the radium room. Cleaning women, perhaps wisely, would be reluctant to go in; residents lacked experience and could not always be trusted to handle the radium; physicists would not demean themselves and were too busy at their desks with "research", "dosimetry", and teaching aspects of radium to actually physically handle the stuff. Thus, much of the work in the radium room became a do-it-yourself proposition for the radiation therapist, or at best a matter of standing over the resident while he did it with the usual ineptness. Another distasteful aspect of the radium room was the cleaning off and disassembling of used applicators, most of which were offensive, malodorous, and generally nauseating to handle.

The answer to all this, of course, is a radium technician (preferably an elderly gentleman post prostatectomy, and therefore unlikely to reproduce his kind) who will relieve the radiation therapist of many of the radium room chores and might well be the equivalent to the therapist of several inches of lead protection for certain of his important organs and tissues. Radium room technicians, properly educated, can actually enjoy working in the radiation room, and have been known to derive a certain pleasure and satisfaction from lugging heavy radium containers around the place.

The afterloading system described previously (1) is a combination of two basic ideas: the presterilized disposable plastic applicator and the prefabricated permanent cesium 137 cartridge assembly. Putting these two ideas together saves a lot of effort and fuss in the routine treatment of certain tumors of the female genital tract. As an added bonus, the substitution of cesium 137 for radium drastically reduces protection and storage requirements, indeed eliminates the need for a radium room.

The presterilized, disposable, plastic applicator was conceived and designed in prepollution days when disposability was still a virtue, and recycling unheard of. Nowadays, one supposes, the applicator should be constructed of biodegradable plastic. Disposability, nonetheless, has much to recommend it - including less cost in money, time, and effort, and elimination of need to handle unpleasant, smelly, unhygienic applicators covered as they usually are in blood and corruption.

The total equipment required for the cesium afterloading system is contained in a small carrying case something like the one shown in figure 1. This case measures about 18x9x6 inches and weighs about 40 pounds. It contains a permanent storage safe for approximately 250 mg radium equivalent of cesium 137, has space for all the instruments, charts, plastic plugs, solvent, etc. It can be carried to the bedside for loading and unloading. There is nothing to be sterilized, cleaned, or manipulated, the case requires only occasional dusting with a damp rag to remove cobwebs and keep it socially clean. It can be stored almost anywhere. Figure 2 shows the case open, the charts required fixed within the lid. Also seen is a small bottle containing solvent and a few simple handling tools. Figure 3 shows another version of the same kind of portable cesium safe.

The basic construction of the cartridge, shown in figure 4, consists of a series of sources that can be of almost any desired strength, separated by ball bearings; the rest of the cartridge is made up of speedometer cable, and is encased in a metal mesh tubing. The whole assembly is very flexible. There is a groove code and a color code on the handle for identification purposes. A view of various handles or shanks for a variety of cartridges is shown in figure 5. The ungrooved portion of the handle is important in the technique of removing the cartridge from the plastic disposable applicator, it is the portion gripped by a special instrument as the plastic tube surrounding it is cut. Figure 6 is a radiograph of an actual set of cesium source cartridges, appropriately labeled with the source arrays and strength and the active length for the uterine cartridges. The vaginal cartridges are single sources, and are considered point sources for dosimetry purposes. The whole group of cartridges (roughly 250 mgm radium equivalent) can be permanently housed in the portable carrying case shown in figure 3.

Figure 7 shows the chart summarizing information for cartridge identification and specification that is included in the portable carrying case containing the safe. The time correction chart is shown in figure 8. It is only necessary to read off the date to obtain the correction factor by which the withdrawal time (calculated as for radium) needs to be multiplied. A good lifespan for a set of cesium sources would be 10 years. If calibrated at approximately 14 percent above nominal value at the outset, after 5 years they will be at nominal value; after a further 5 years they will be approximately 14 percent below nominal value, and ready for trade-in.

The simple handling tools shown in figure 9 can be used to transfer the cartridges rapidly from safe to patient, and vice versa. A pair of scissors (not illustrated) have been modified to act somewhat like wire strippers to cut the plastic tubing around the cartridge. At the same time it grips the smooth part of the shank of the cartridge, enabling it to be rapidly withdrawn from the applicator within the patient and returned immediately to its home in the portable safe.

The disposable plastic applicator is shown in figure 10. Three different packages are available. One contains vaginal cylinders with lead, anteriorly and posteriorly, for protection of the rectum and bladder; one contains lead on one side only, generally used for rectal protection; and one contains no lead.

Plastic vaginal cylinders are shown in figure 11. If these are too large to fit into the vagina, or if there is a contraction due to scarring or tumor, these applicators can be pared down with a knife or scissors and custom fitted to the tumor. Light stainless steel springs are used to hold the vaginal cylinders apart. The collar on the intrauterine tube is a friction fit and can be moved up and down the tube, depending on the length of the uterine cavity. The plastic is fairly stiff, although flexible enough so that if there is sharp anteversion and/or anteflexion of the uterus, the tube would conform without kinking. Two of the plastic tubes containing cartridges are shown in figure 10. Plugs have been applied in the distal opening of the tubes to retain the cartridge in position. These plugs normally are applied by dipping in the solvent cyclohexanone, pushing them into the ends of the tubes. The seal is instantaneous and permanent. In order to remove the cartridges, the plastic has to be cut in the region of the shank of the cartridge using special "wire-stripper"-type scissors.

Figure 12 shows the assembled applicator within a patient. Note that vaginal applicators without lead have been used (although anterior and posterior lead for rectal and bladder protection is shown in the accompaning diagram). Note also that the groove code on the cartridge handles is very easily seen, for identification purposes.

Figure 13 demonstrates that the plastic applicators can generally be well seen on plain radiographs. In this illustration the vaginal cylinders are used with lead, both posteriorly and anteriorly, and wire springs are used to space the vaginal cylinders into the fornices.

Figure 14 shows a rather different situation. Since there was very little room, it was decided to use lead posteriorly only for rectal protection. The vaginal cylinders had to be pared down to fit into the small vaginal vault.

Figure 15 shows a stump carcinoma case. The length of the stump was about 2 cm, and there was very little space at the vault for vaginal sources. Note that springs have not been used for separation, and the vaginal cylinders have been pared down to make them fit. Under these circumstances, a linear source can be used that extends from the cervical stump to the upper part of the vagina.

Figure 16 shows a similar situation. The cervical stump remnant has been almost completely destroyed by tumor.

Figure 17 shows (left) poor application of vaginal cylinders partly due to distortion by tumor. Consequently, only the intrauterine tandem was loaded with radioactive sources. Subsequently a better application of the vaginal part of the assembly was achieved (right), and this subsequently was loaded.

Figure 18 shows a patient with a large submucosal fibroid, to illustrate the flexibility of the tubing and cartridge within the uterine cavity.

A considerable amount of work has been done on the comparative dosimetry of cesium, radium, and cobalt 60 using all manner of techniques in both water and solid phantom materials, and different dosimeters. Figures 19 and 20 show comparisons of radium and cesium dosimetry made with Isodensitometer survey of film exposed in solid phantom material. It can be seen that radium and cesium dose distributions are very similar for the two different kinds of applicators.

Cesium 137 for intracavitary or interstitial use has certain well known advantages. They can be summarized as follows:

1. 660 K.V. monoenergetic gamma emission
2. Fission product, therefore abundant and inexpensive
3. Long half-life (26.6 years)
4. Protection and storage is simpler than with radium or cobalt 60
5. Available in physically and chemically inert form (3M microspheres)
6. No gaseous daughter product such as radon (c.f. radium)
7. No problem of helium buildup and possible rupture of capsule (c.f. radium)
8. Reduced hazard to personnel in the event of a "spill" or accident. Cleanup under such circumstances is easy since the cesium is in the form of a dense milky-white powder incorporated in ceramic material. It cannot be inhaled, even if ingested will pass through the gastrointestinal tract without being absorbed.

In terms of protection of nursing personnel, the ordinary bedside lead shield is far more effective for cesium than for equivalent amounts of radium. Figure 21 shows measurements made around the bed using equivalent amounts of radium and cesium. A 1 inch lead screen is placed at the bedside (figure 22) and measurements again are made. They show that, for practical purposes, the exposure working behind this type of shield is approximately half as much for cesium as it is for radium (figure 23).

Clinical considerations in relation to this technique would indicate that reactions, cure-rates, dosimetric considerations, etc. are precisely the same for cesium 137 as for radium, assuming that similar methods are used. It would be almost impossible to prove that the cesium 137 treatment is equivalent to the radium treatment, if indeed such proof were necessary.

At the University of Cincinnati College of Medicine both general radiology residents and a few residents in "straight" radiation therapy have been trained. Stress is laid on dosimetry, and it has been considered important to offer residents an opportunity to observe various techniques and applicators in radium and cesium therapy, rather than try and indoctrinate them to the superiority of any particular type of equipment. Therefore, among other things, this cesium system has been used, also a modified Manchester radium system and also the Fletcher applicator (initially without afterloading, more recently with afterloading).

A total of 41 cases of carcinoma of the cervix have been treated, using the cesium afterloading technique with more than a 3-year followup. The first cases were treated about 9 years ago. Of these 41 cases, 18 are dead; 12 died of carcinoma of the cervix, 2 of metastatic carcinoma of the breast, and 1 each of cardiac failure, metastatic carcinoma of the parotid, pneumonia, and stroke. Two patients with Stage I disease, uncontrolled, were lost; one Stage II disease, uncontrolled; four Stage III; and five Stage IV. It should be mentioned that initially there was a tendency to use the cesium afterloading system on more advanced cases. There is one patient, initially Stage II, currently alive with active disease at 2 1/2 years. The pelvis seems to have done well and gives her no symptoms, but she has distant metastases (lungs, Virchow's node, etc.). There are 22 cases alive and well 3 years or more: 14 Stage I, 5 Stage II; 2 Stage III, and 1 Stage IV (biopsy proved bladder involvement). There are five Stage I cases alive and well between 5 and 8 years, three Stage II, one Stage III, and one Stage IV -- all beyond 5 years.

Complications have been similar to those expected with standard radium techniques. Four patients experienced rectal reactions, 2 of whom had strictures (one requiring a colostomy that may be permanent). One patient had a radiation cystitis that subsided and did not become fistulous. No patients have experienced either bowel, ureter, or bladder fistula. One developed small bowel obstruction about 4 weeks after her cesium treatment was completed. At laparotomy, a loop of small bowel was adherent to the uterine fundus. It is possible that there might have been a perforation of the fundus at the time of the sounding and dilation of the cervix, but this was not suspected in the operating room. It is also possible that the distal cesium source was in close proximity to the peritoneal cavity in the region of the fundus. In any event, the patient made an uneventful recovery following corrective surgery and is now well, with no clinical evidence of neoplasm.

We have had three minor misadventures in relation to the plastic applicators.

On one occasion the small plastic seal at the distal end of the uterine tandem was lost within the patient, but later was expelled spontaneously. Its dislodgement did allow secretions to get into the plastic tube and onto the cartridge, and presented us with an irritating chore cleaning the cartridge.

A stainless steel spring unknowingly was left in the vagina of one patient for a period of about 6 weeks. When seen by residents for followup, she complained of discharge and pain although pelvic examinations were made, the spring somehow was not discovered. Finally it was shown on x ray, quite deeply embedded in the tissues. After removal the patient seemed none the worse, indeed she is an 8 year survivor with no evidence of recurrence.

One of our patients dislodged the equipment by pulling it out during a period of confusion. This, of course, can happen with almost any kind of equipment that protrudes from the patient.

SUMMARY

The afterloading system described above using disposable plastic applicators and prefabricated permanent cesium 137 source assemblies has worked out very well in practice. The small portable lead safe and associated small items contained in a carrying case are the only permanent equipment; together with a packaged sterilized disposable plastic applicator, they comprise the entire armamentariam for carrying out the treatment. The need for a radium room has been eliminated. The practical aspects of treatment, results, and clinical reactions are identical with those experienced with any of the routine methods using radium. The reduction in work, fuss, and mess, and in radiation exposure for the therapist, technicians, nurses, and other personnel, has been considerable.

Improvements in the system have been made by Dr. Delouche in Paris, (2,3). He has devised a simple plastic clamp that maintains the applicators in one of a series of fixed geometric configurations, standard dose distribution charts have been worked out for each configuration, thus diminishing the need for routine elaborate dose calculations for each individual patient.

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3. DELOUCHE, G.: La curietherapie gynecologique endocavitaire par Caesium 137. J Radiol Electr 48: No. 5, 229-242, 1967.

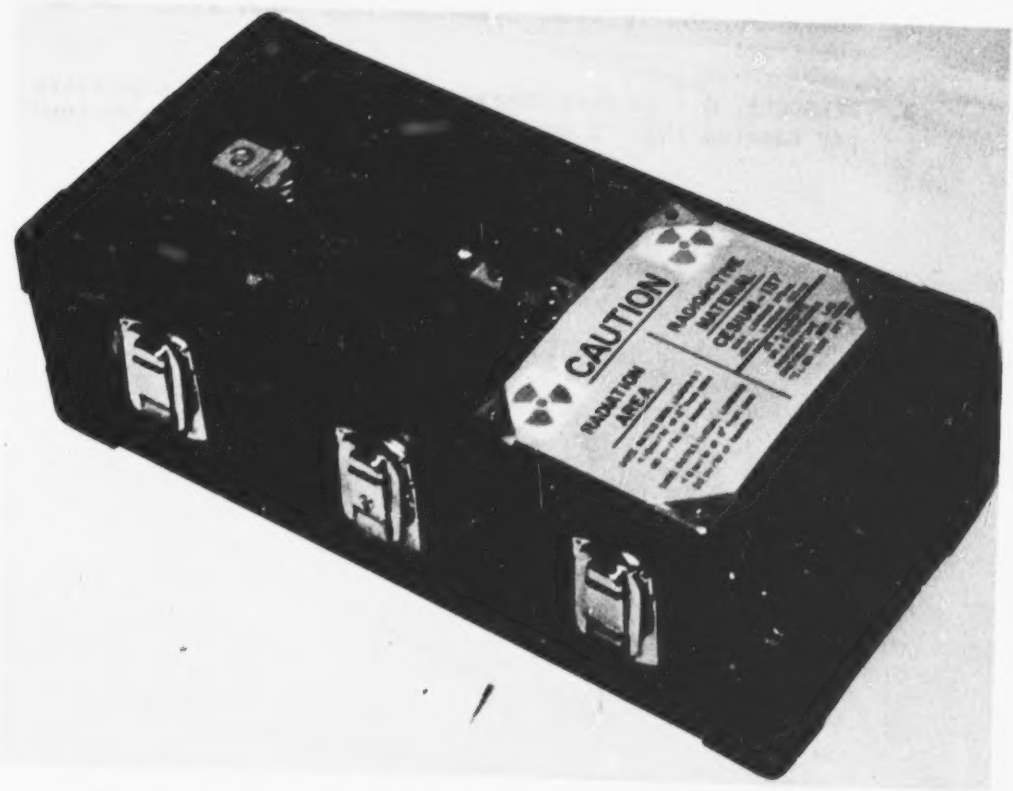
CAUTION
RADIATION AREA
RADIOACTIVE MATERIAL
CESIUM-137

Figure 1. Carrying case for cesium afterloading system.

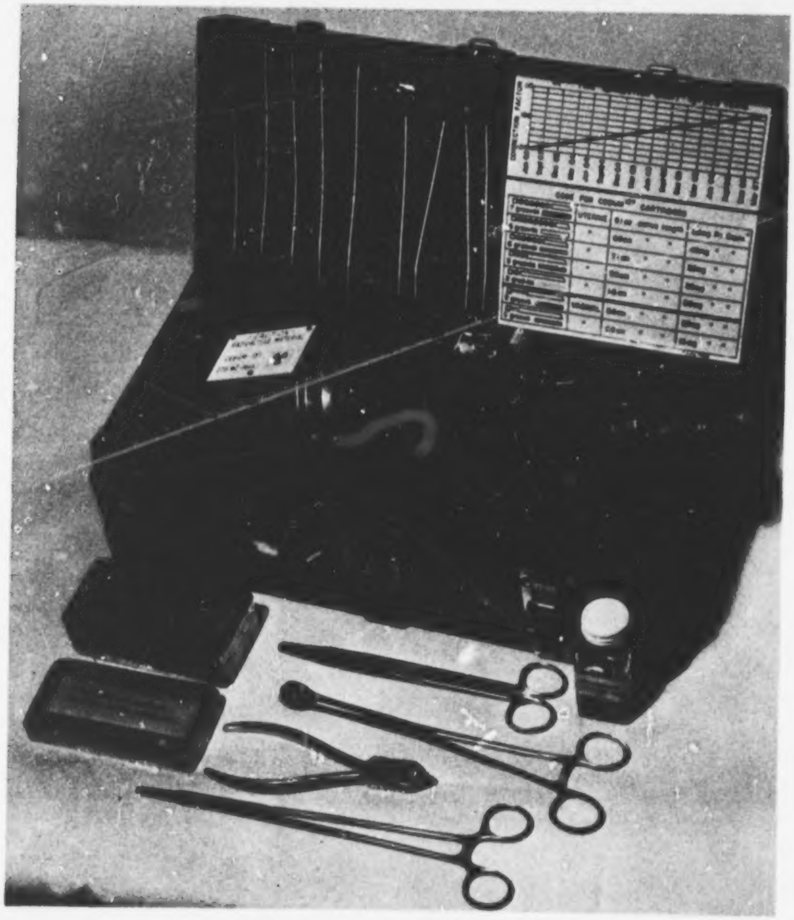

Figure 2. Carrying case for cesium afterloading system, open; necessary charts fixed inside lid.

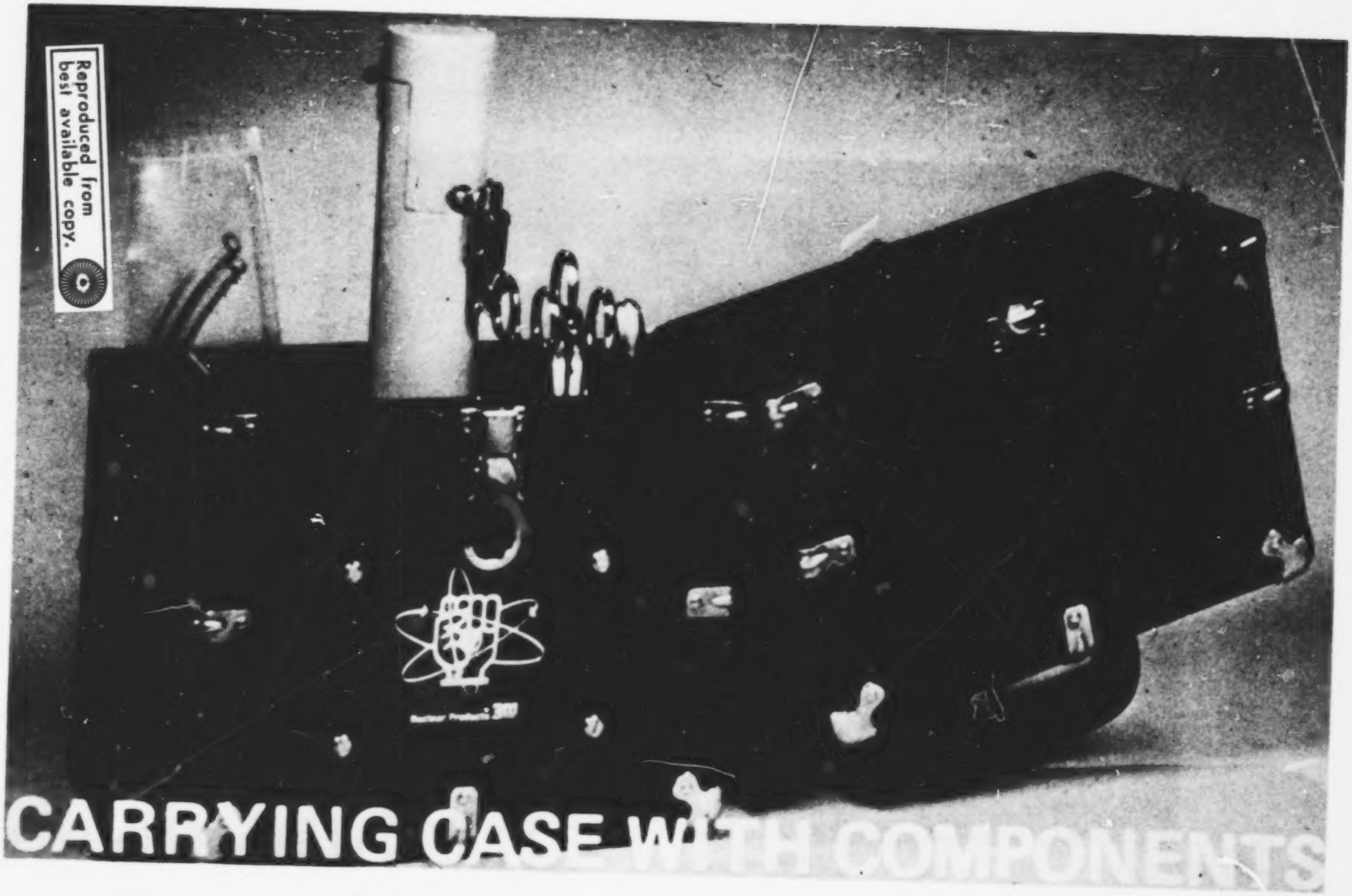
CARRYING CASE WITH COMPONENTS

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Figure 3. Another version of the cesium safe.

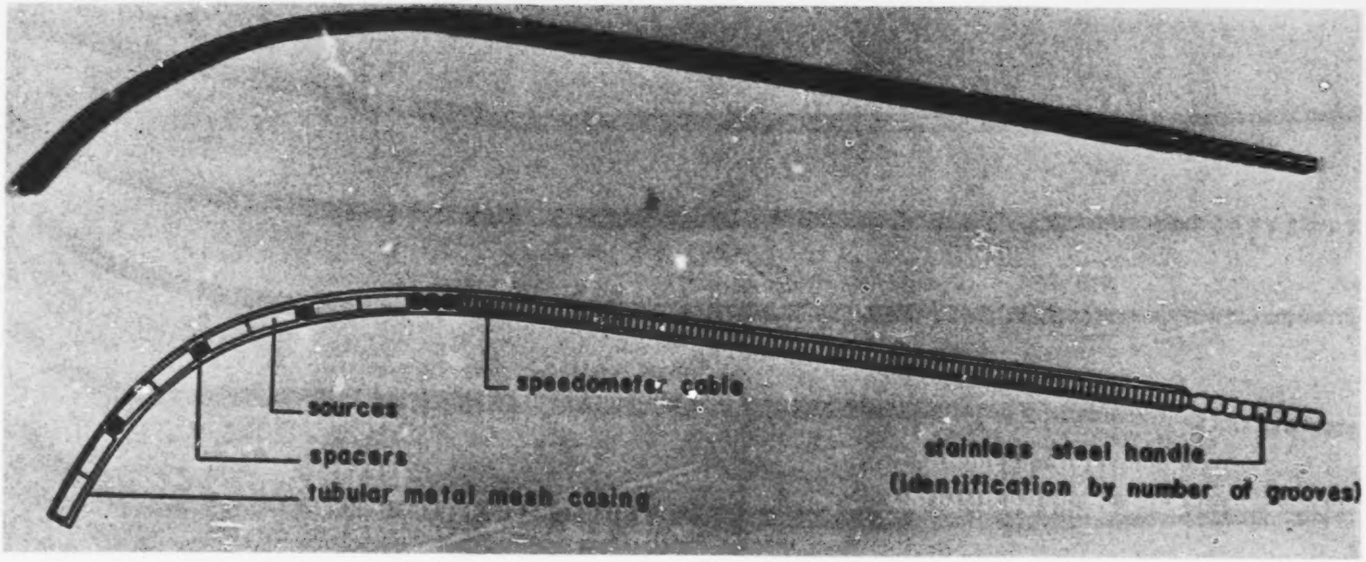

speedometer cable
sources
spacers
tubular metal mesh casing
stainless steel handle
(identification by number of grooves)

Figure 4. Typical source cartridge (intrauterine type).

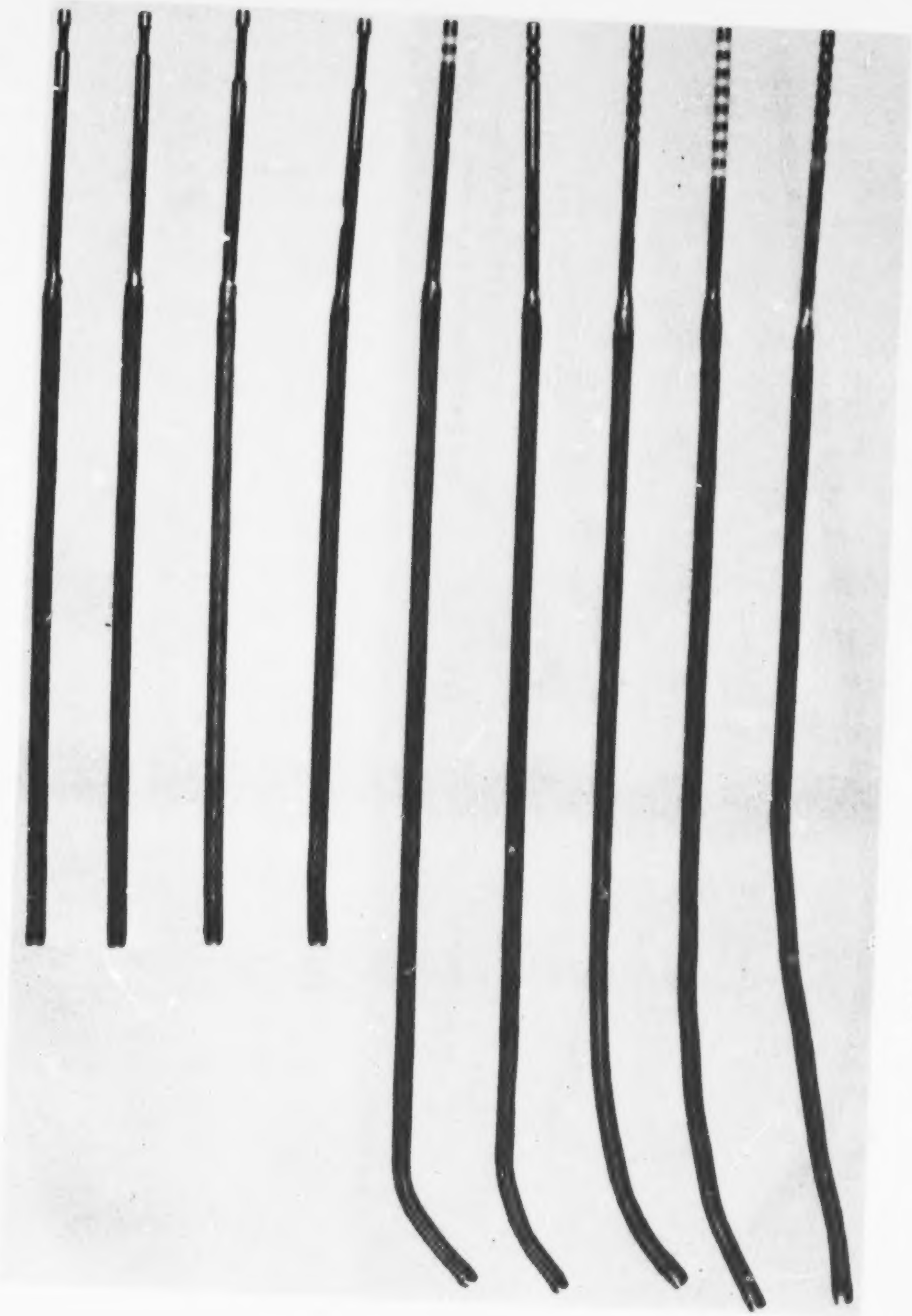


Figure 5. Handles (or shanks) for various cartridges.

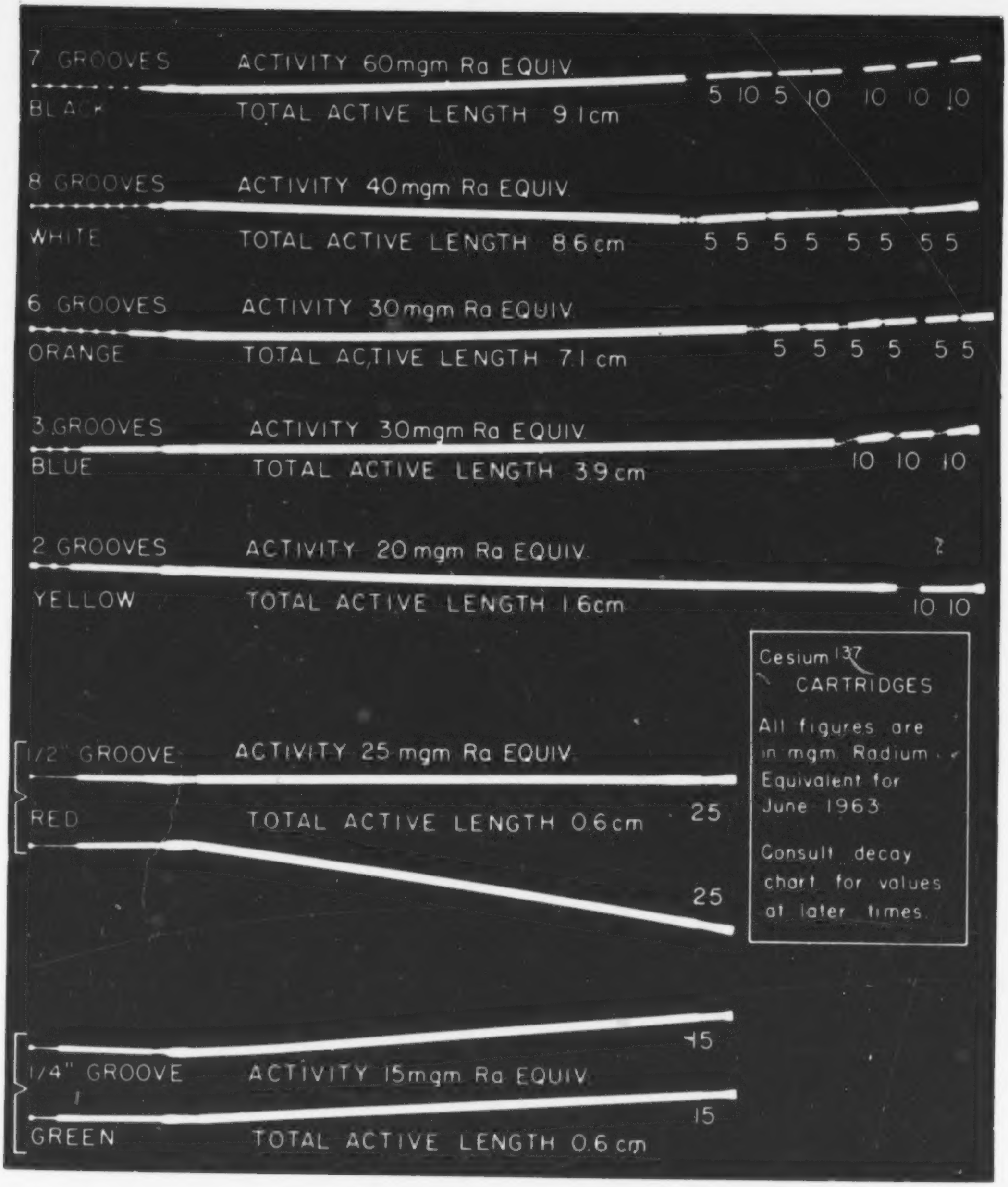
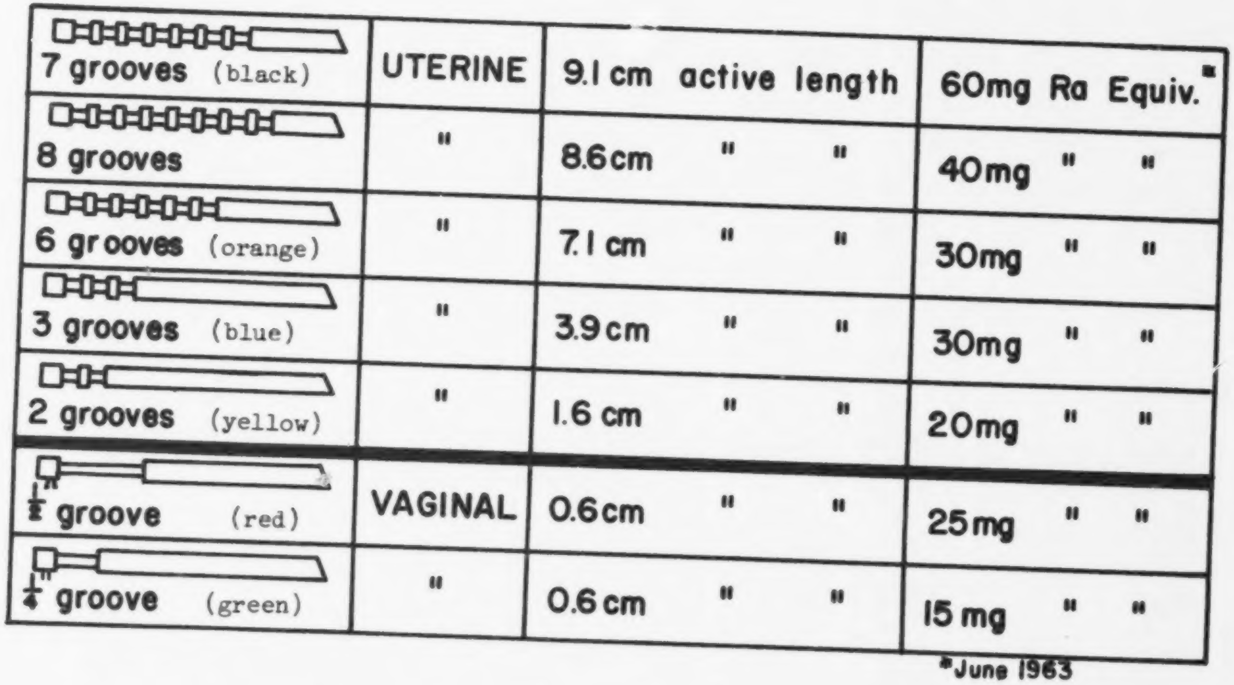

7 GROOVES
ACTIVITY 60mgm Ra EQUIV
BLACK
TOTAL ACTIVE LENGTH 9.1cm
5 10 5 10 10 10 10
8 GROOVES
ACTIVITY 40mgm Ra EQUIV
WHITE
TOTAL ACTIVE LENGTH 8.6cm
5 5 5 5 5 5 5 5
6 GROOVES
ACTIVITY 30mgm Ra EQUIV
ORANGE
TOTAL ACTIVE LENGTH 7.1cm
5 5 5 5 5 5
3 GROOVES
ACTIVITY 30mgm Ra EQUIV
BLUE
TOTAL ACTIVE LENGTH 3.9cm
10 10 10
2 GROOVES
ACTIVITY 20mgm Ra EQUIV
YELLOW
TOTAL ACTIVE LENGTH 1.6cm
10 10
Cesium 137 CARTRIDGES
All figures are in mgm Radium Equivalent for June 1963
Consult decay chart for values at later times
1/2" GROOVE
ACTIVITY 25mgm Ra EQUIV
RED
TOTAL ACTIVE LENGTH 0.6cm
25
25
15
1/4" GROOVE
ACTIVITY 15mgm Ra EQUIV
GREEN
TOTAL ACTIVE LENGTH 0.6cm
15

Figure 6. An actual set of cesium source cartridges, appropriately labeled.



7 grooves (black)	UTERINE	9.1 cm active length	60mg Ra Equiv.*
8 grooves	"	8.6cm " "	40mg " "
6 grooves (orange)	"	7.1 cm " "	30mg " "
3 grooves (blue)	"	3.9cm " "	30mg " "
2 grooves (yellow)	"	1.6 cm " "	20mg " "
½ groove (red)	VAGINAL	0.6cm " "	25mg " "
¼ groove (green)	"	0.6cm " "	15 mg " "

*June 1963

Figure 7. Code for cesium 137 cartridges.

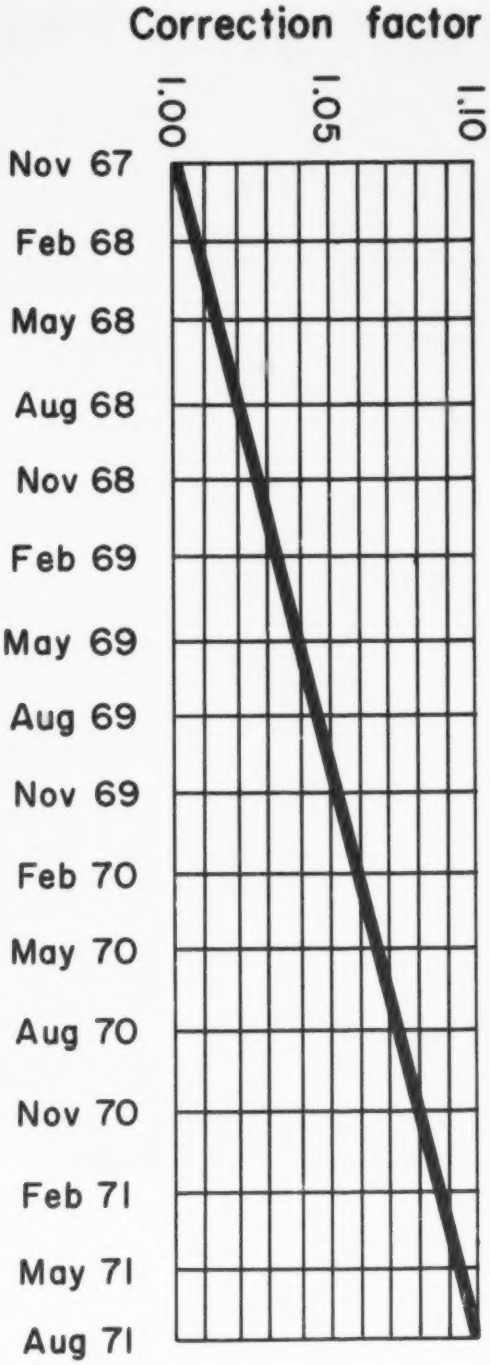


Figure 8. Time correction chart for cesium 137 (T 1/2 = 26.6 years).

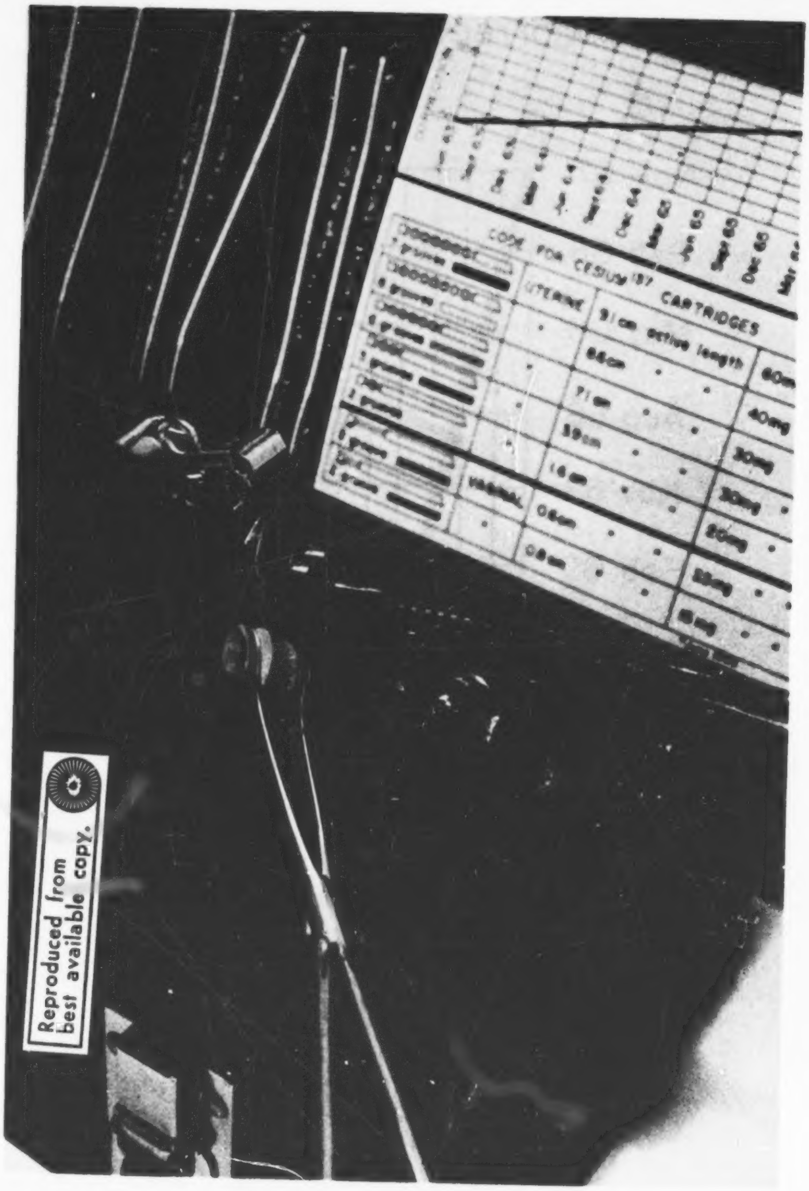

CODE FOR CESIUM 137 CARTRIDGES
UTERINE
VAGINAL
91cm active length
86cm
71cm
59cm
16cm
06cm
60mg
40mg
30mg
30mg
20mg
Dec 64
Mar 65
Jun 65
Sept 65
Dec 65

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Figure 9. Handling tools for cartridge transfer.

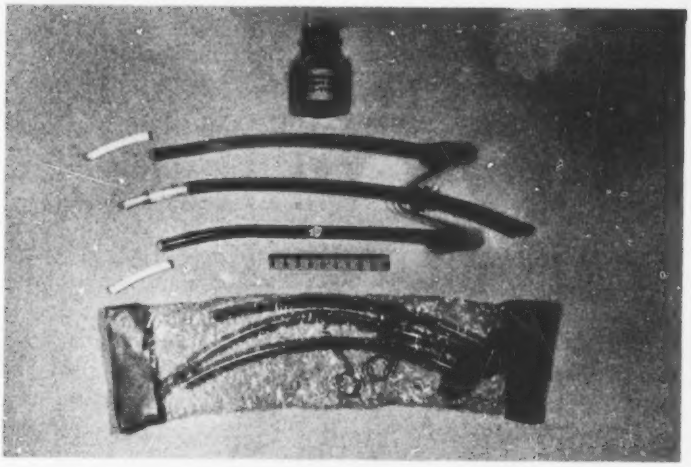

Figure 10. Disposable plastic applicator.

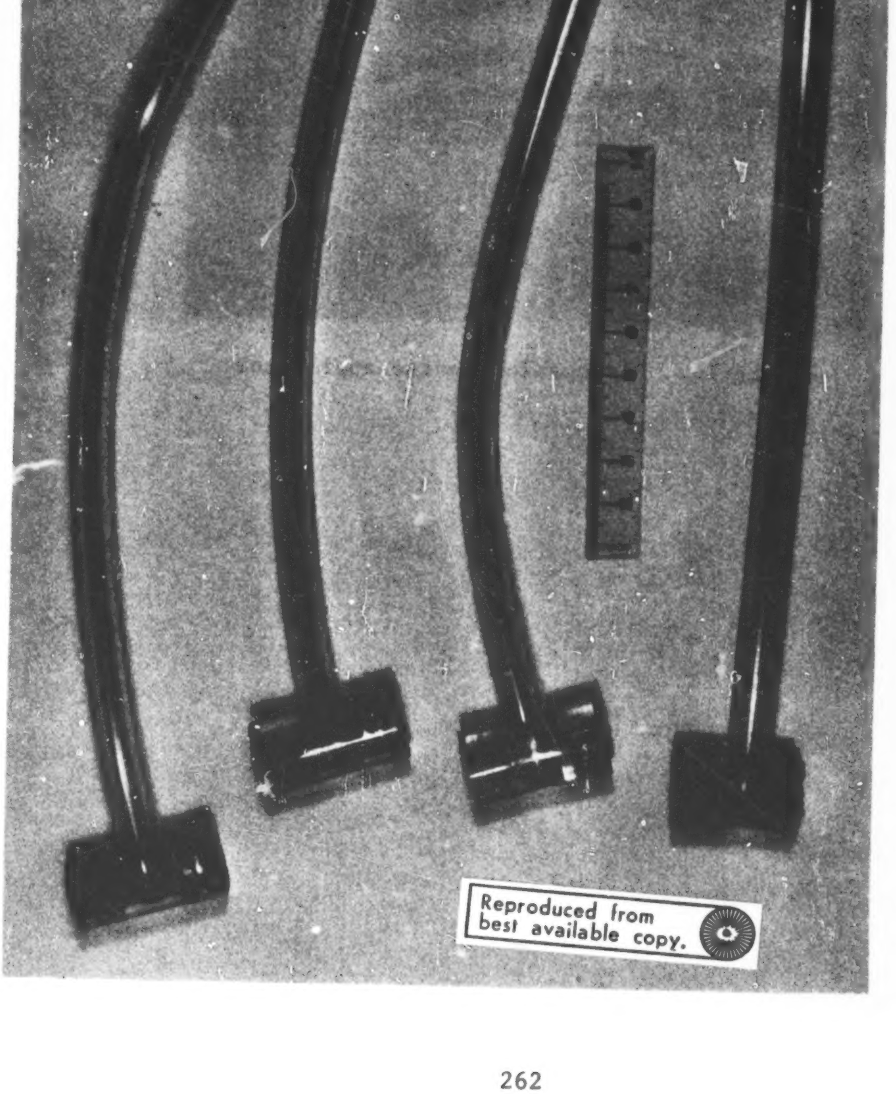

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Figure 11. Plastic vaginal cylinders.

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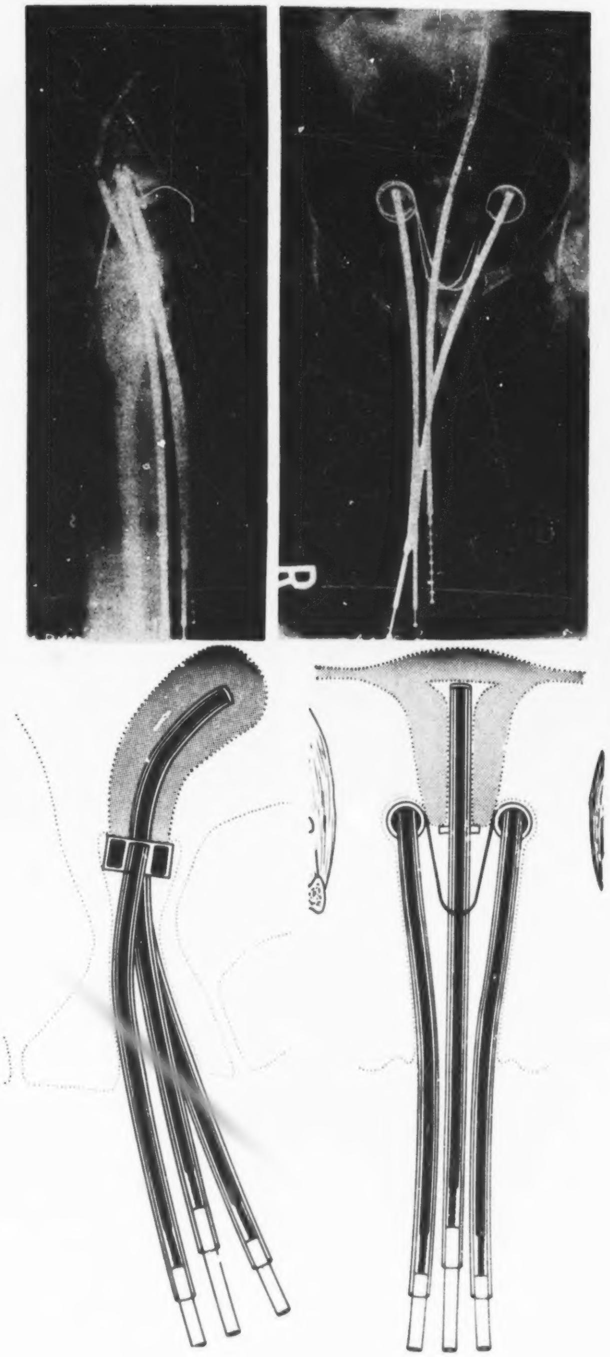

Figure 12. Applicator assembled within patient.

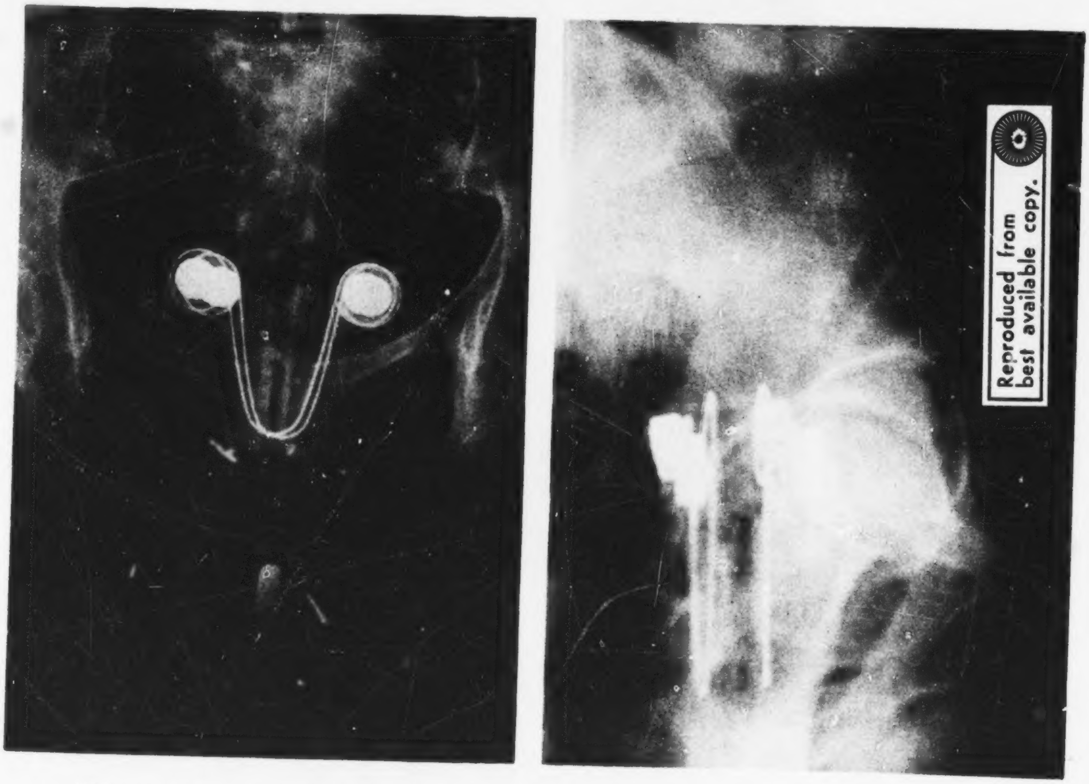

Figure 13. Vaginal cylinders, with anterior and posterior lead.

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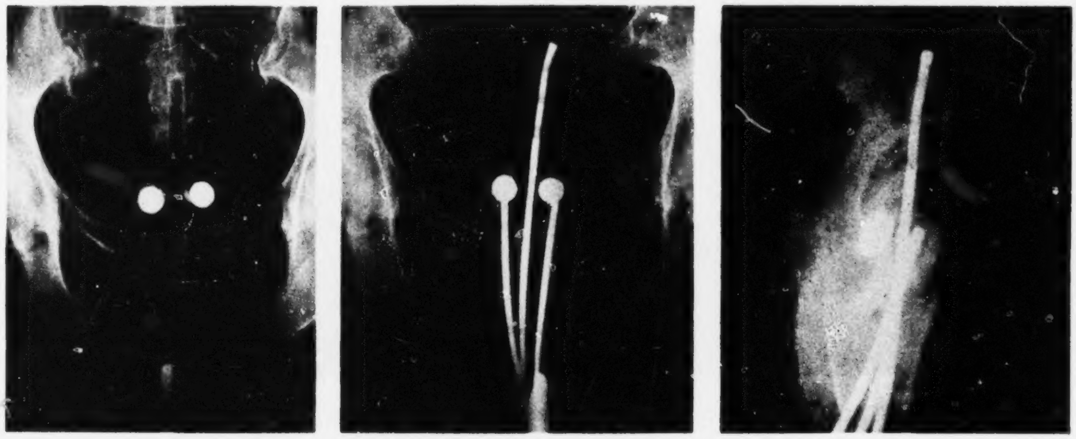

Figure 14. Vaginal cylinders with posterior lead.

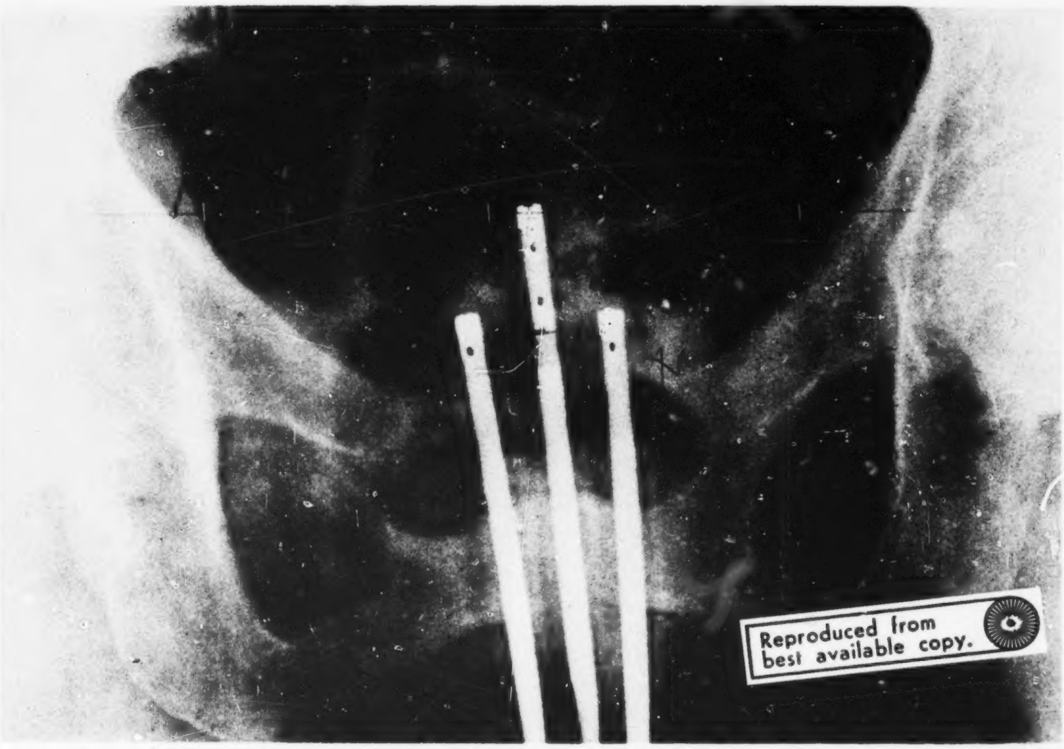

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Figure 15. Afterload cylinders in a stump carcinoma.

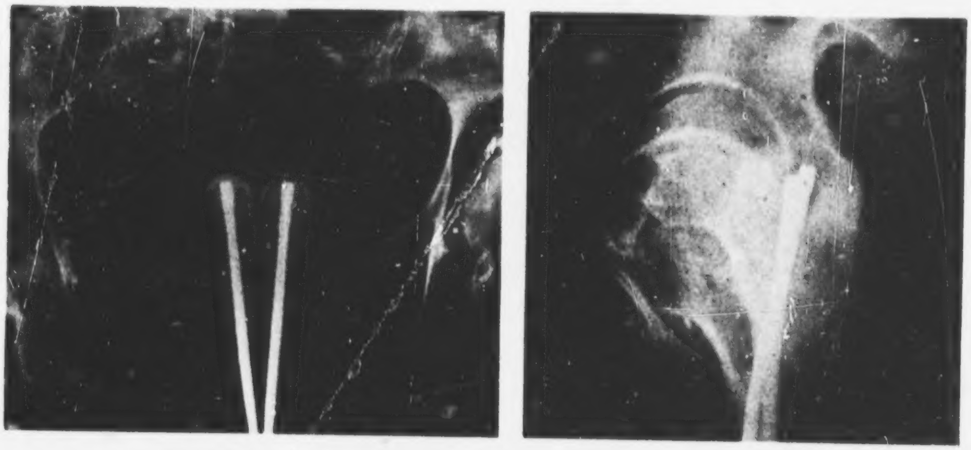

Figure 16. Cervical stump remnant almost completely destroyed by tumor.

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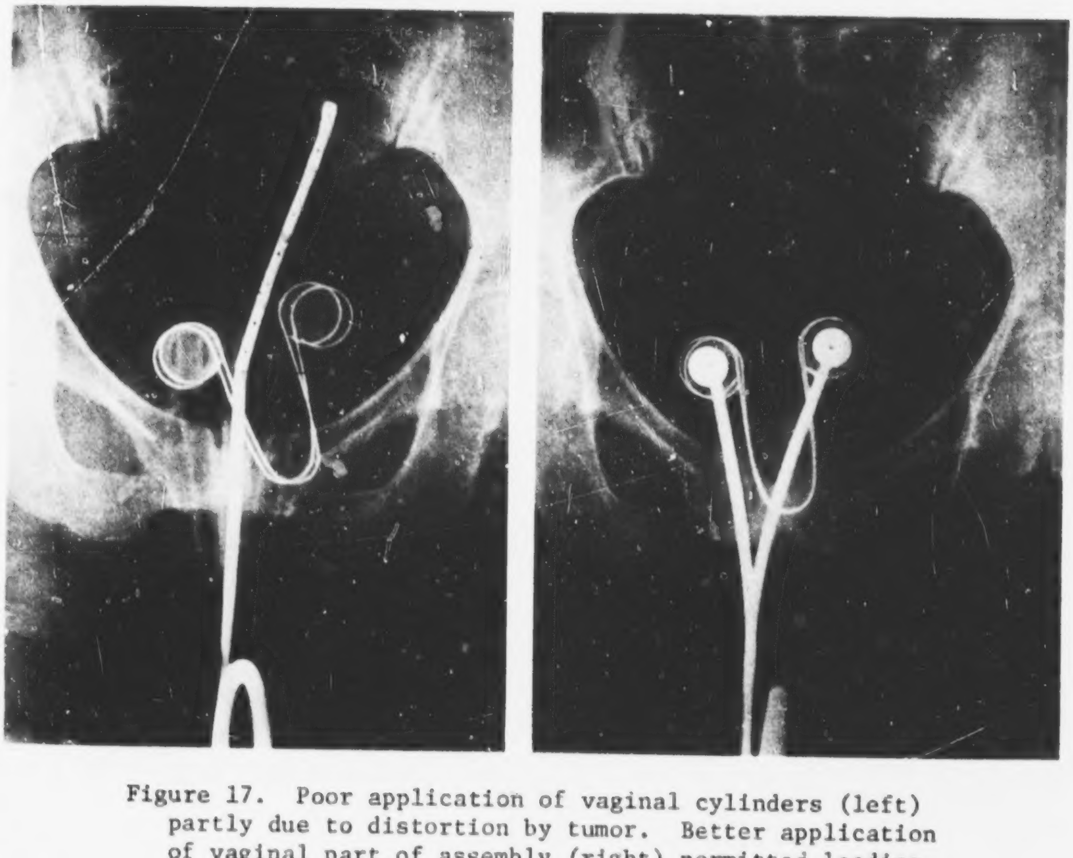

Figure 17. Poor application of vaginal cylinders (left) partly due to distortion by tumor. Better application of vaginal part of assembly (right) permitted loading.

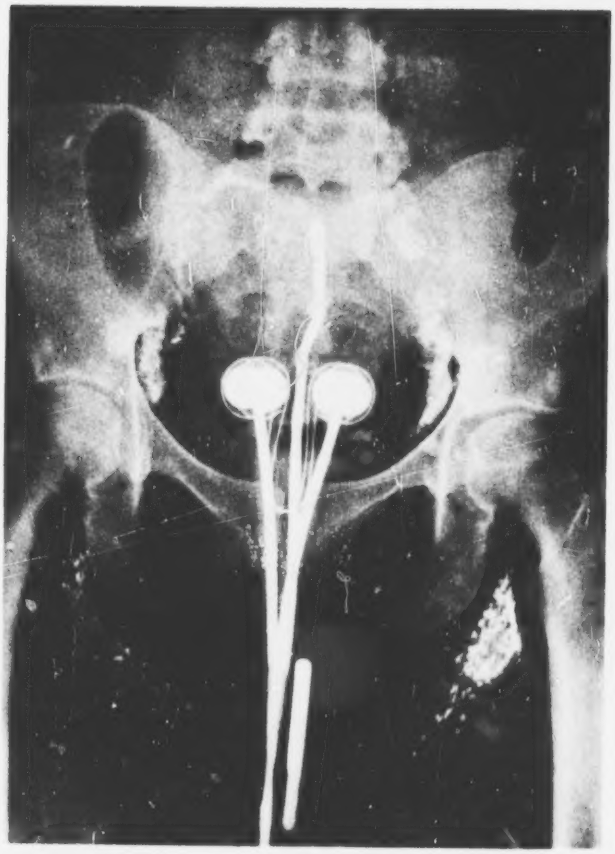

Figure 18. Large submucosal fibroid.

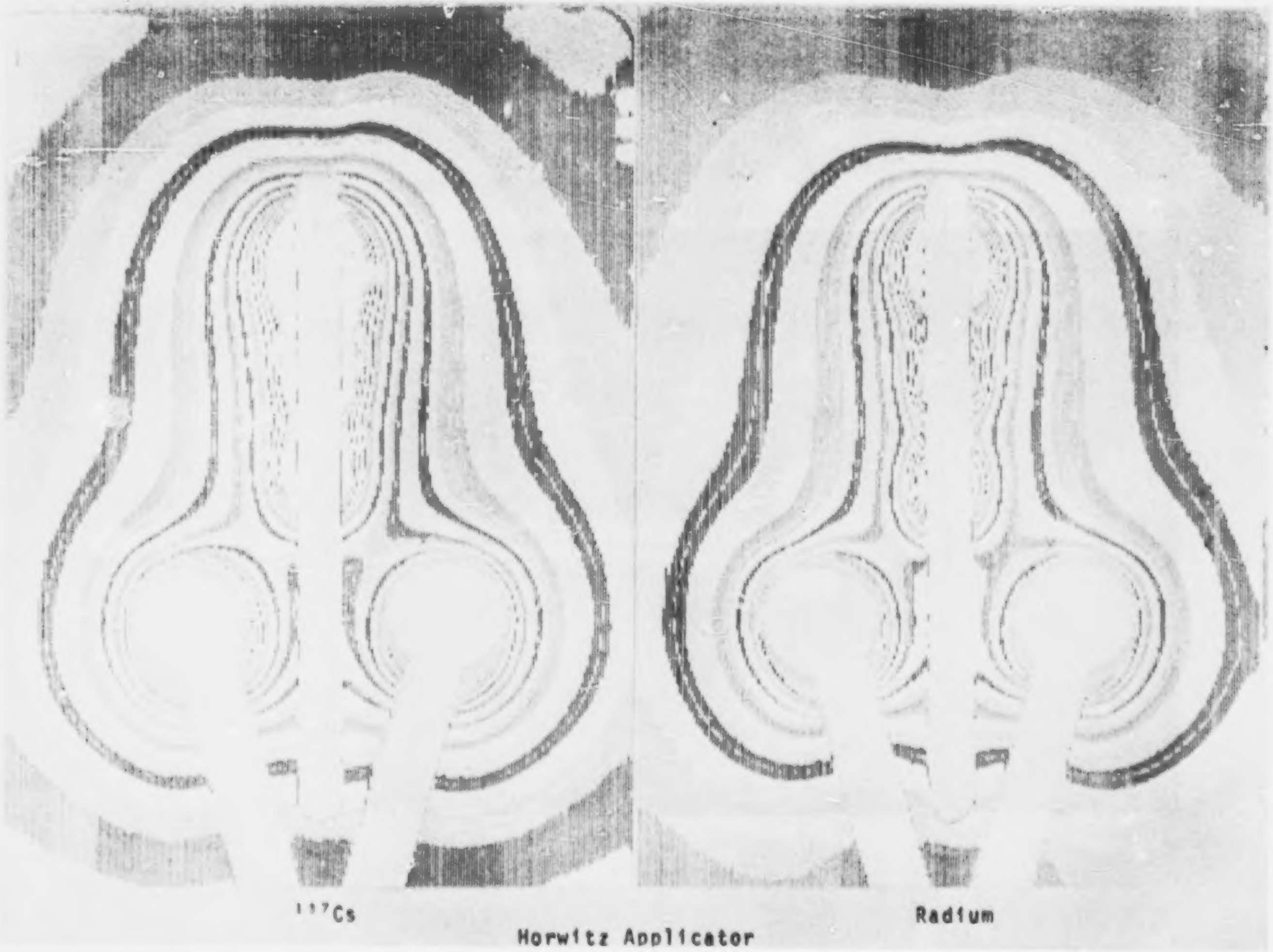
^{137}Cs
Radium
Horwitz Applicator

Figure 19. Comparison of radium and cesium dosimetry.

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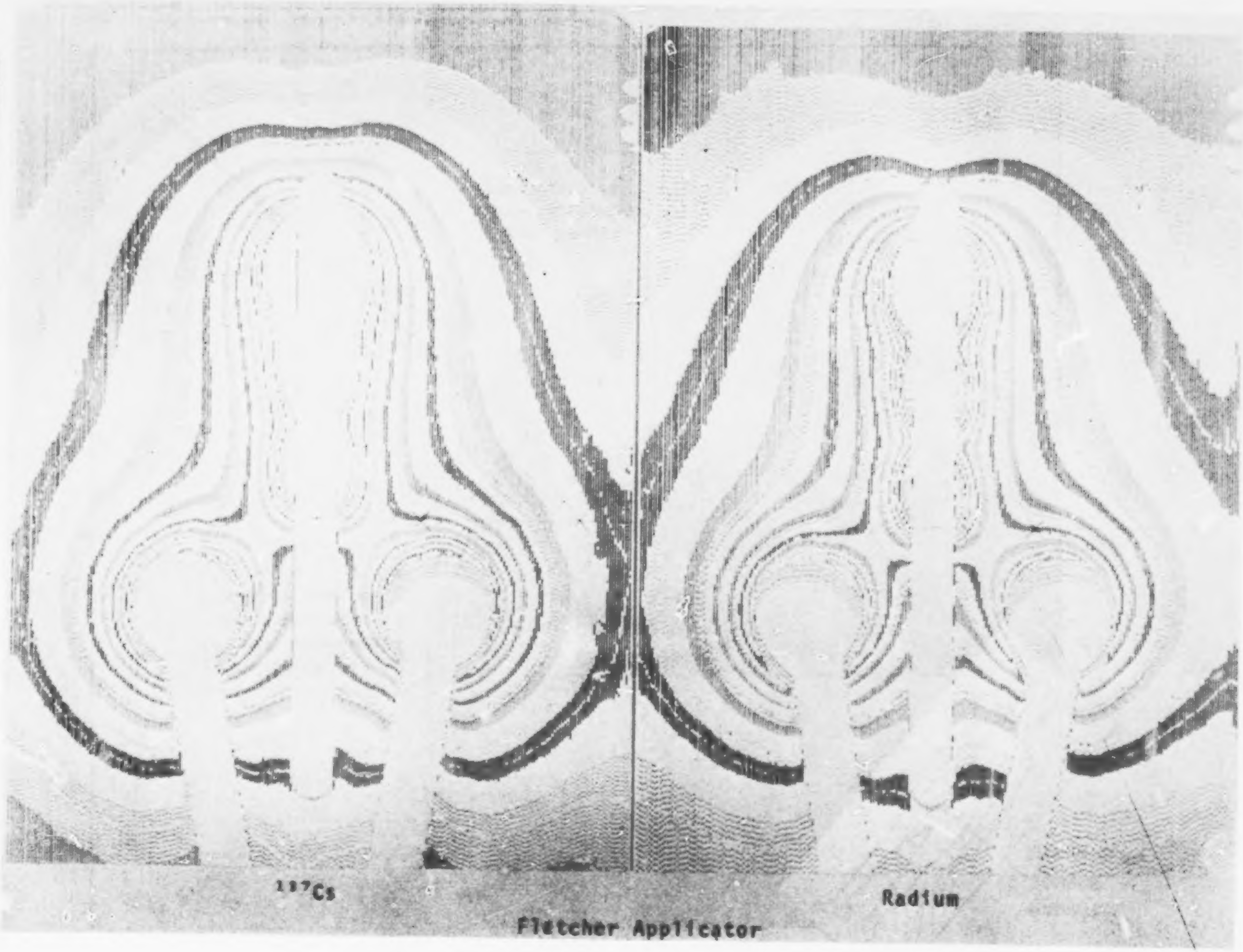

Figure 20. Comparison of radium and cesium dosimetry.

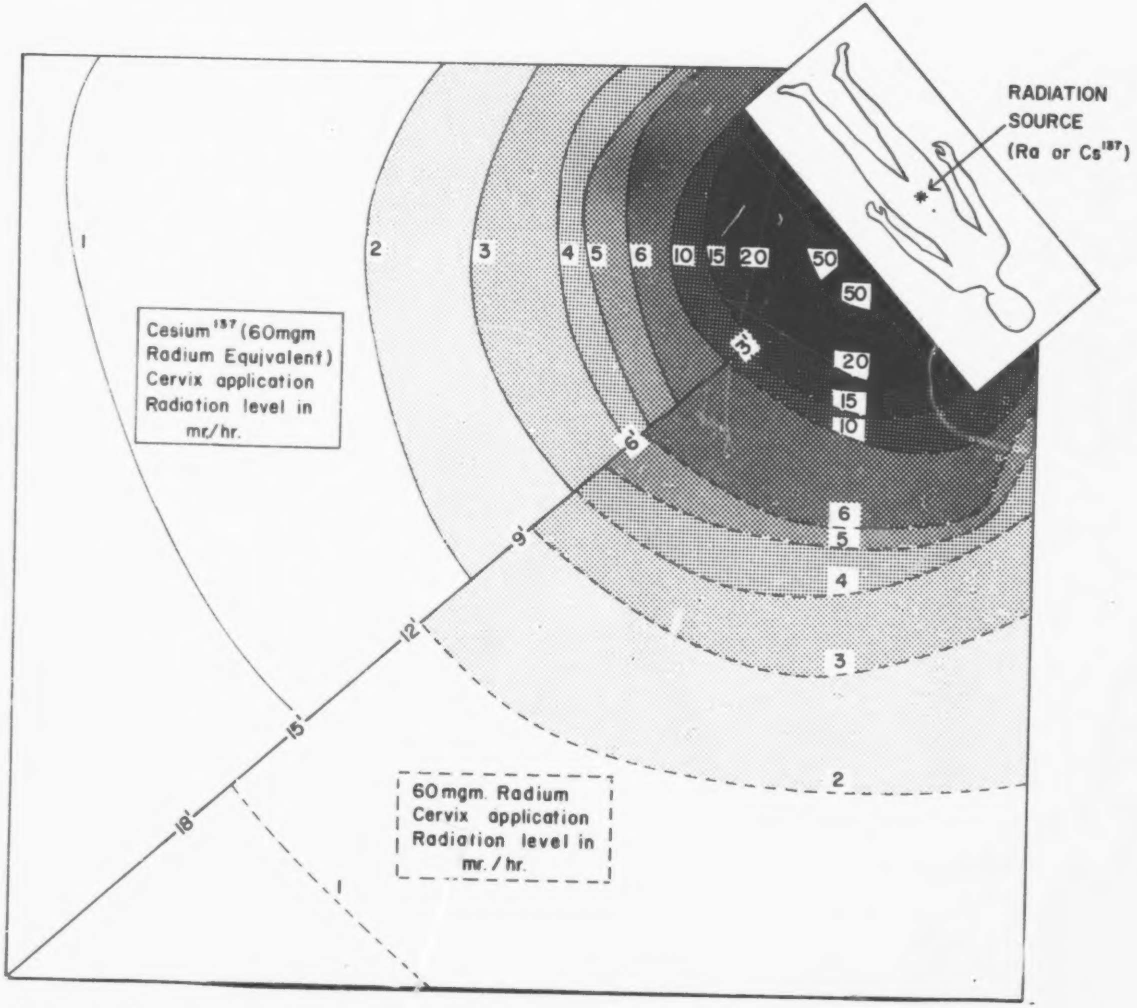
RADIATION
SOURCE
(Ra or Cs^{137})
1
2
3
4
5
6
10
15
20
50
50
15
20
15
10
6
5
4
3
2
1
6'
9'
12'
15'
18'
Cesium^{137} (60mgm
Radium Equivalent)
Cervix application
Radiation level in
mr/hr.
60 mgm. Radium
Cervix application
Radiation level in
mr./hr.

Figure 21. Measurements around bed, using equivalent amounts of radium and cesium.

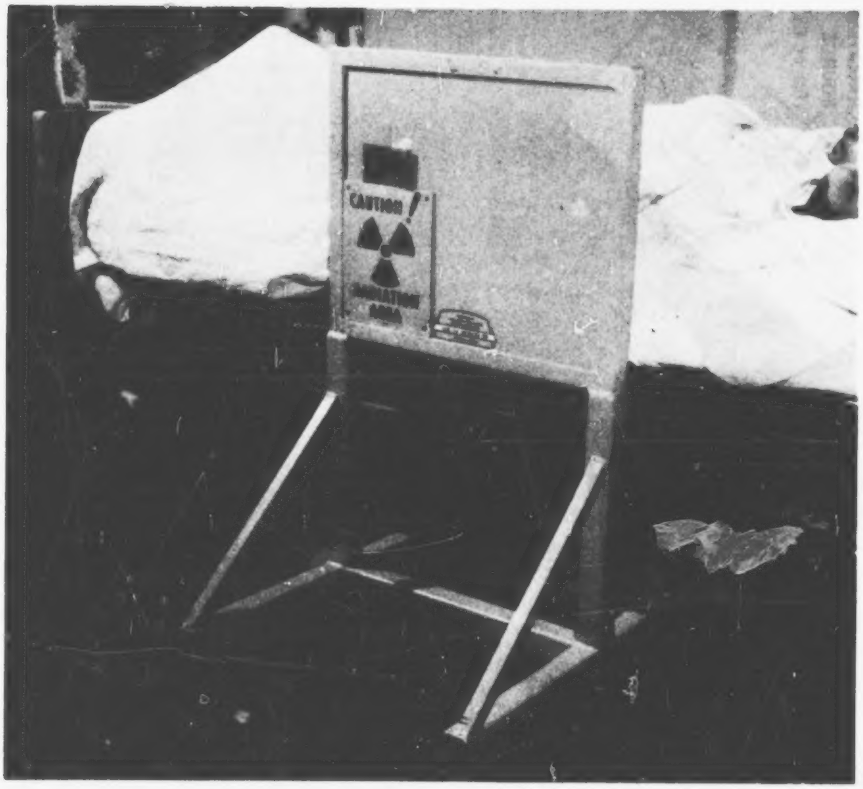
CAUTION!
RADIATION AREA

Figure 22. One-inch lead screen installed at bedside.

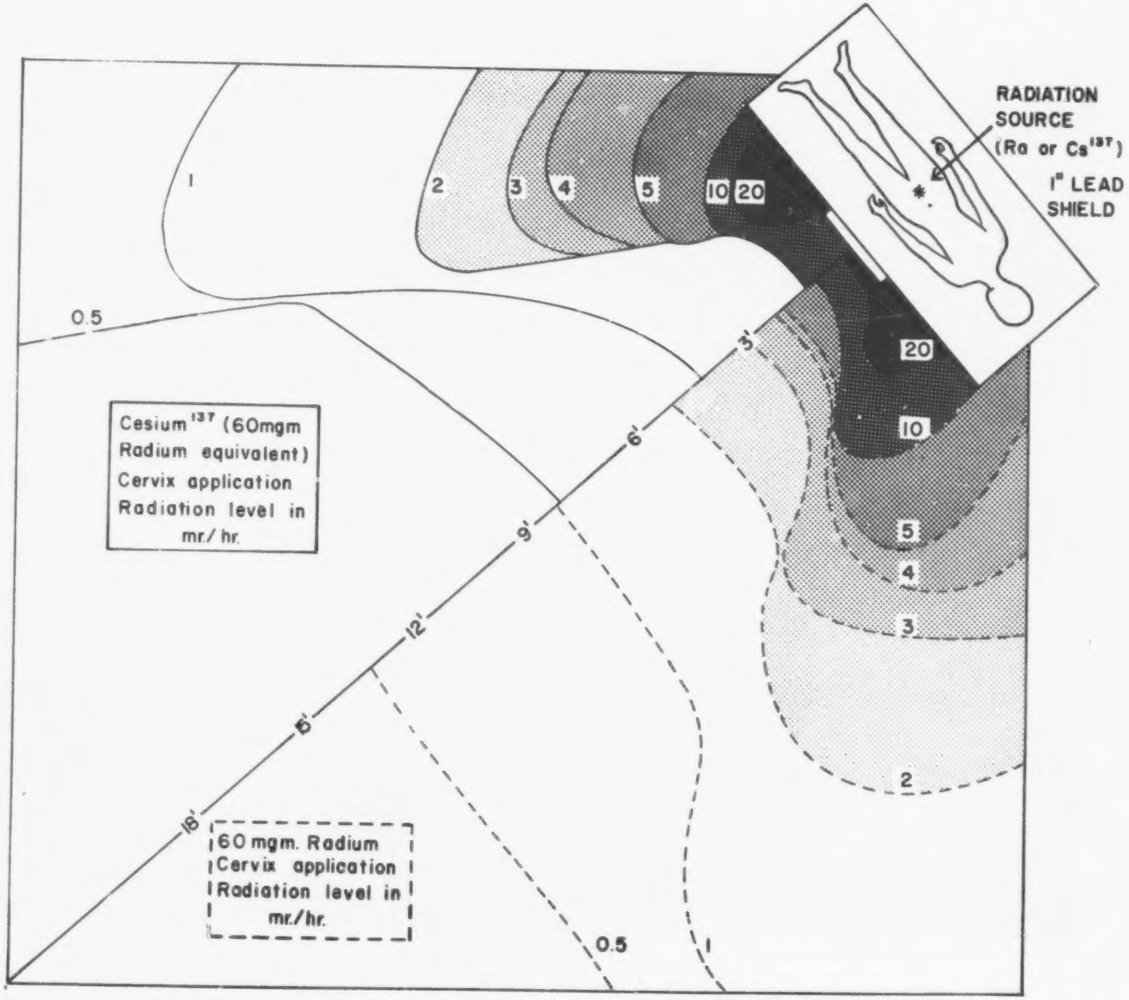

Figure 23. Comparative exposure, working with cesium behind lead screen.

REDUCTION OF RADIATION EXPOSURE WITH AFTERLOADING MINIATURIZED SOURCES IN CERVIX CANCER

Sidney M. Silverstone, M.D., Norman Simon, M.D.,
and L. C. Roach, M.D.

In the administration of radium therapy for cancer of the cervix uteri, gamma radiation is an ever-present risk to medical and paramedical personnel, to other patients, and to visitors. The total radiation exposure in the treatment of a single case is much more than is realized. Many factors cannot be measured or calculated; an unknown number of persons are affected without their knowledge or consent.

ANALYSIS OF RADIATION EXPOSURE

Assuming that radium storage facilities are adequate and safe, and that all necessary instruments are available for the handling of radium, we find radiation exposure in the following phases of the procedure:

1. Preparation of the Radium Applicators

Preparation of the intrauterine and vaginal applicators involves close range handling of the radium sources, even with long-handled forceps and other special instruments. Speed of handling is desirable, but is acquired only after experience. Little accidents, such as dropping a radium capsule or missing the thread of a screw in some of the devices, add to the exposure, even if they occur infrequently. Radiation exposure to fingers, if the radium source should be so handled, can be higher than 5,000 mR per minute for a 10-mg capsule. It is not expected that anyone would be so rash as to pick up a radium capsule with his fingers, but if he is threading a needle or loading a tandem or placing a screwhead over a radium container, he can unwittingly bring his fingers dangerously close to the radium. Furthermore, radium capsules must be removed from the drawers in the radium safe, and this often is done at awkward angles that can easily lead to such accidents as dropping the capsules on the work table, hopefully not on the floor.

While the radiotherapist peers over the work table with his face 30 to 40 cm from the radium, the lens of each eye receives 1 mR per minute for every 10-mg radium capsule exposed.

2. Sterilization

Sterilization must be done by a cold method such as gas or immersion in a bactericidal solution. Heating methods such as boiling, autoclaving, or flaming are far too dangerous, especially with old capsules of radium in which there is an accumulation of helium and other gases under pressure. Accidents have occurred in which boiling was left unattended with resulting explosion of the overheated radium capsule and dispersion of radon gas all over the hospital. The method of sterilization at the present time is to place the loaded devices in the drawer of a heavily leaded cart. The drawer is lined with stainless steel and filled with a bactericidal solution sufficient to cover the devices completely. The radium cart then is transferred to the operating room for the next phase.

3. Transportation

The 5 cm thickness of lead surrounding the drawer of the radium cart reduces exposure from 100 mg of radium to 5 mR per hour at 1 meter distance. However, exposure at the handle of the drawer is as high as 10 to 35 mR per minute, which is the dose the hand would receive.

From the radium room to the operating room, the individual who wheels the cart, the elevator operator, and whoever else is in the elevator at the time will get general body irradiation at the rate of 5 mR per hour per 100 mg of radium at 1 meter. In the operating room, the radium cart usually is placed in a spot that presumably has the least amount of traffic.

4. Operating Room

In the operating room, dilatation of the cervix, insertion of the tandem in the uterus, and insertion of vaginal applicators in the vaginal vault is a procedure that takes from 20 to 45 minutes, and usually is done under general anesthesia. During this procedure, the radium is withdrawn from its protective lead cart to be placed in the patient. There is no protective lead screen, therefore not only the operator but all personnel in the operating room are exposed. After the operation the patient herself becomes a source of radiation exposure to everyone near her in the traffic encountered during the trip from the operating room to recovery room to the patient's room.

5. X-Ray Studies

Roentgenograms of the pelvis with stereo antero-posterior and lateral views are made to check the position of the radium sources. During transport to and from the x-ray department and her stay there, the patient is a source of radiation. Therefore the roentgenograms should be made expeditiously, not only because of radiation exposure to other individuals but also the fogging effect on x-ray film.

6. Patient Care

In her room, the patient is a constant source of radiation. At a distance of 2 meters from a patient treated with radium for 5,000 mg hrs the dose is 1,000 mR. The patient should not only be in a room by herself, but the distance between her and the patient in the next room must be checked -- notwithstanding the wall between them -- and the exposure dose monitored. Visitors can be reduced to a minimum, or eliminated if necessary; nursing and medical care should be monitored with either film badges or integrating dosimeters. Bedpans should be used for all urinary and bowel excretions, to guard against accidental loss of radium.

7. Removal of the Radium Applicators

Removal of the radium applicators involves exposure to personnel in close proximity. There is additional exposure from cleaning the applicators for gross removal of secretions before they are placed in the radium cart. In the return to the radium room, the same risks apply as originally in the transportation of the radium to the operating room.

8. Dismantling

There is about as much exposure in dismantling the applicators as there was in their construction. Occasionally there is unexpected difficulty removing the radium capsules from various devices, and the extra minutes involved add to the radiation exposure.

EARLY ATTEMPTS AT RADIATION REDUCTION

It was clear to many radiotherapists that the conventional use of radium in the treatment of cervix cancer was attended by too many risks of radiation exposure and that drastic improvements were necessary.

To improve safety in handling, Silverstone (1) and Fletcher, Shalek, Wall and Bloedorn (2) devised colpostats with long handles. Silverstone (3) devised a stainless steel intrauterine tandem which contained the radium permanently, thereby eliminating need for loading and dismantling. Subsequently, afterloading techniques were developed by Suit, Moore, Fletcher and Worsnop (4) and by Henschke (5), all of whom used radium. Horwitz, Kereiakes, Bahr and Cluxton (6) developed an afterloading technique utilizing cesium 137, but their cesium sources were dimensionally the same as radium sources. The major disadvantage of the radium sources, in addition to the inherent risks of radium itself, was their dimensional thickness which greatly limited their useful applications. It was only when thin cobalt 60 and cesium 137 sources became available that a broader and more useful adaptation of these sources for the treatment of cancer of the cervix could be made.

THE THIN PLASTIC TANDEM

It was possible to obtain a cobalt 60 source in the form of a wire thin enough to be contained within the lumen of an 18-gauge needle. The needle fit the lumen of a thin plastic tube with an outside diameter of 2 mm or less. Thus a tandem was constructed of the plastic tube with an inactive 18 gauge needle wire in its lumen (figure 1). A semicircular stop was placed on this tandem at a point 6 cm from the end of the plastic tube, corresponding with the position of the external os of the cervix. The plastic tu[illegible] about 30 to 40 cm long, and inactive wire are sterilized by the gas method.

The plastic tandem with its inactive wire is inserted into the uterine cavity in the usual manner. Since anesthesia is not required, the entire procedure can be performed in a properly equipped examining room. The vagina is packed with gauze against the cervical stop to maintain the tandem in position; the distal end of the tandem emerging from the introitus is taped to the inner thigh; a Foley catheter is inserted into the bladder; roentgenograms are taken to check the position of the wire. Then -- and not until then -- the inactive wire is removed and replaced by a similar wire containing cobalt 60 in its first 6 cm. Up to this point there has been no radiation exposure. The transfer of the active wire is made quickly, within a few seconds, by one individual without disturbing the setup. It can be done in the patient's room, in an examining room, or in the x-ray diagnostic room of the radiotherapy department if another roentgenogram is to be taken. The cobalt 60 wire is left in situ for the requisite length of time. Since the strength of cobalt 60 can be made equivalent to that of the radium usually used, the dose rate is similar. When therapy is completed, the cobalt 60 wire is removed as easily and rapidly as it was inserted and replaced into its lead container. Incidentally, the active cobalt 60 wire does not require sterilization, since technically it is outside the uterine cavity.

VAGINAL APPLICATORS

Cesium 137 can also be miniaturized because of its high specific activity. It is incorporated into thin vycor glass and loaded into the lumen of an 18 gauge needle wire. Our present concentration is 25 mCi, equivalent to 10 mg of radium, in a 1.5 cm length of tubing. Expect to improve this concentration to 1.0 cm. These cesium wires were previously described by Simon (7, 8) for use in his modification of the Heyman capsule for afterloading the uterus for cancer of the corpus. The wire is 30 to 40 cm in length, with the cesium in the first 1.5 cm. It too fits in the lumen of a plastic tube with an outside diameter not exceeding 2 mm.

This cesium wire, with the plastic tube that contains it, is the basic unit with which we have been able to adapt many different types of vaginal applicators to the afterloading technique, including Manchester ovoids (figure 2) and the French (figure 3), Silverstone (figure 4) and Fletcher colpostats. The adaptation requires drilling a hole for the plastic tube at the site where the radium would be placed. The plastic tube then is glued in place with an appropriate bonding agent.

In clinical use, the vaginal applicator with its plastic tubes is placed in the vaginal vault in the usual manner, but with the empty plastic tubes emerging from the introitus. These are taped to the inner thigh. Inactive wires are inserted for x-ray purposes. When ready, the radiotherapist removes the inactive wires and inserts the cesium 137 wires into the plastic tubes without disturbing the vaginal applicator (figure 5). Again, this procedure is done wherever convenient. After the calculated time of application, the cesium 137 wires are removed and returned to their lead storage container.

ADVANTAGES OF AFTERLOADING WITH MINIATURIZED SOURCES

The miniaturized cobalt 60 and cesium 137 sources have greatly simplified the entire system of intracavitary radiation therapy for cancer of the cervix. The radiotherapist continues to employ the same method he has always used, the one with which he is most familiar and has had his best results. He places his applicators in position according to plan, but this time without urgency or fear of exposing himself and others to radiation. He checks the adequacy and accuracy of his setup with impunity. Only when he approves the setup does he activate his system. He is also much freer in the choice of his time of application. In most cases, the entire procedure can be performed in a properly equipped gynecologic examining room.

While both cobalt 60 and cesium 137 are satisfactory for miniaturization, we prefer cesium because its longer half-life, 30 years, simplifies calibration calculations to yearly adjustments. In contrast, cobalt 60 with its half-life of 5.3 years necessitates quarterly adjustments. Another advantage is that cesium's 0.66 MeV gamma ray requires much less protection than the 1.2 MeV gamma ray of the cobalt.

Afterloading techniques have eliminated radiation exposure of personnel incident to preparation, sterilization, operating room, x-ray studies, and dismantling of the applicators. They also have reduced exposure incident to transportation. It is only in loading, unloading, and patient care that some risk of radiation exposure remains. At present there are plans in the making for remote control loading and unloading the afterloaders.

When this has been accomplished, all risks will have been eliminated.

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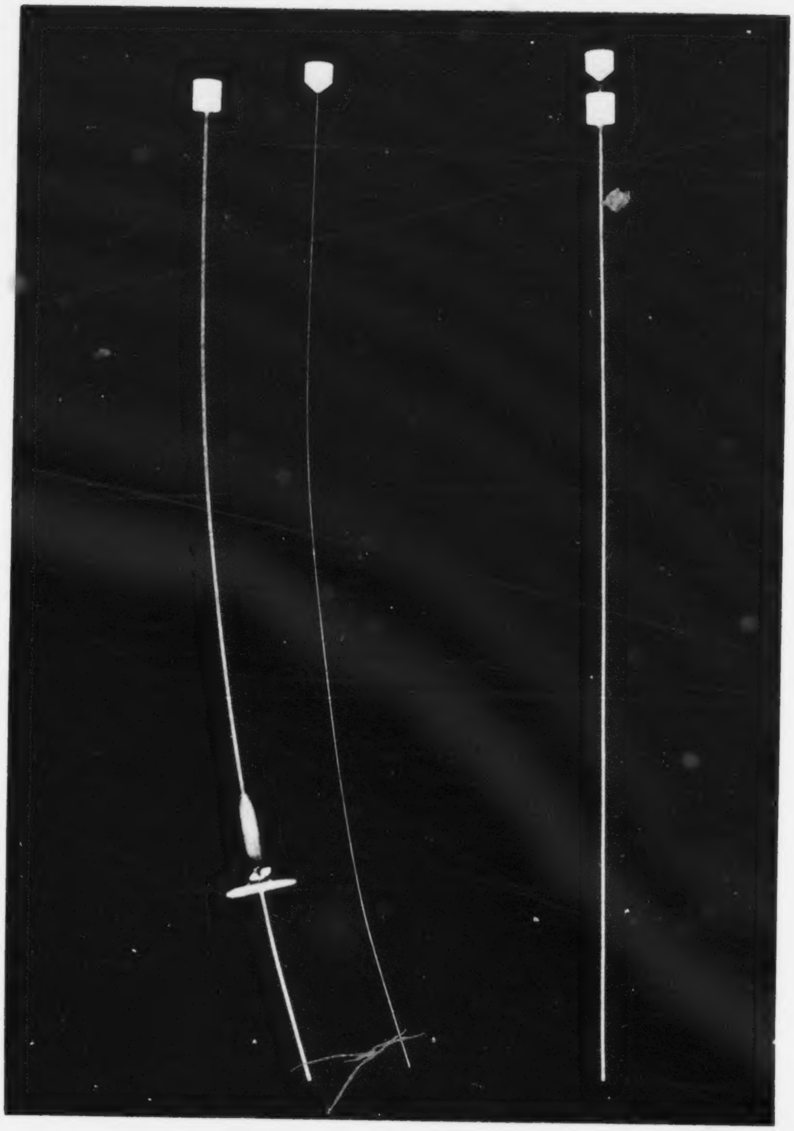

Figure 1. Afterloading tandem.

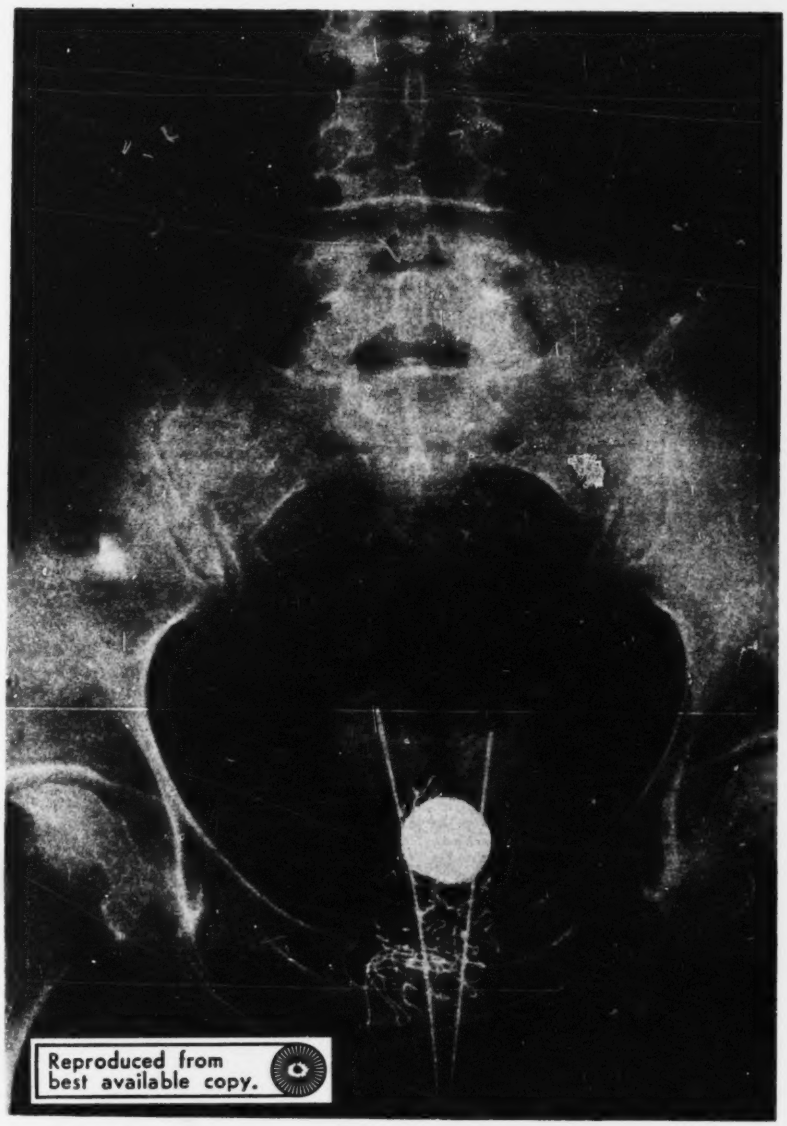
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Figure 2. Afterloaded Manchester ovoids, roentgenogram of pelvis. Dense circle is Foley catheter in bladder.

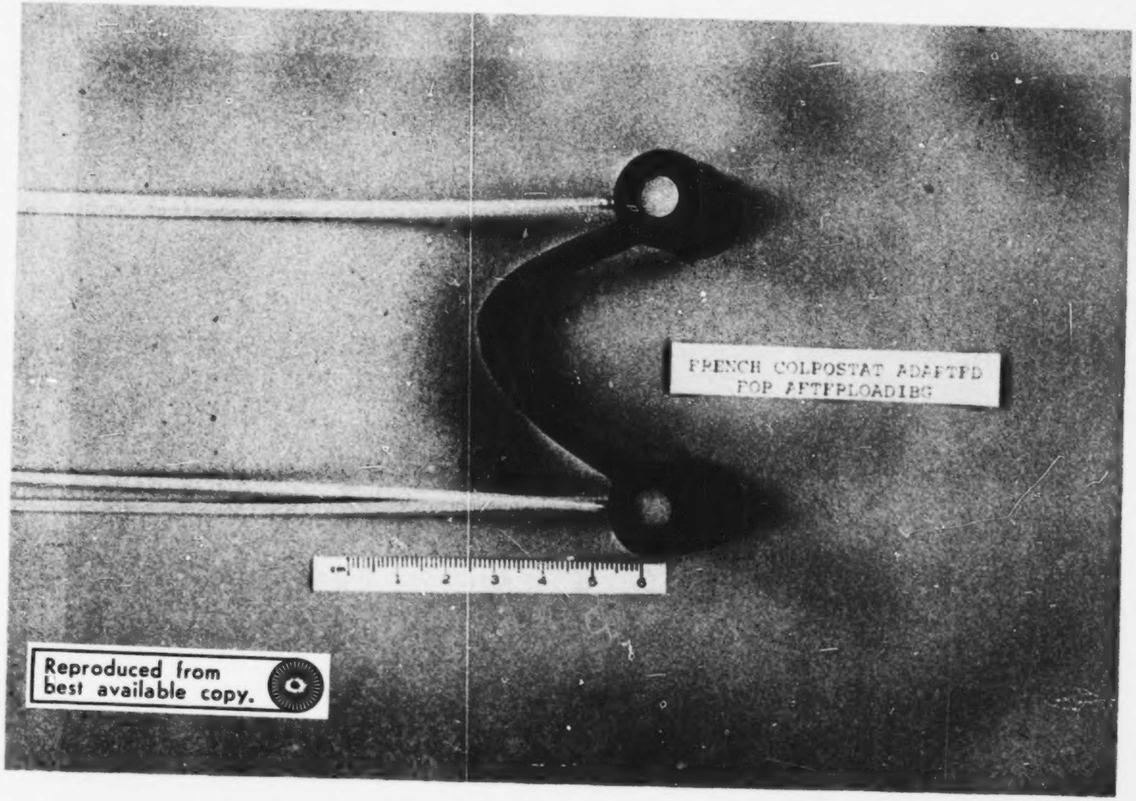
FRENCH COLPOSTAT ADAPTED
FOR AFTERLOADING
cm
1
2
3
4
5
6

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Figure 3. French colpostat adapted for afterloading.

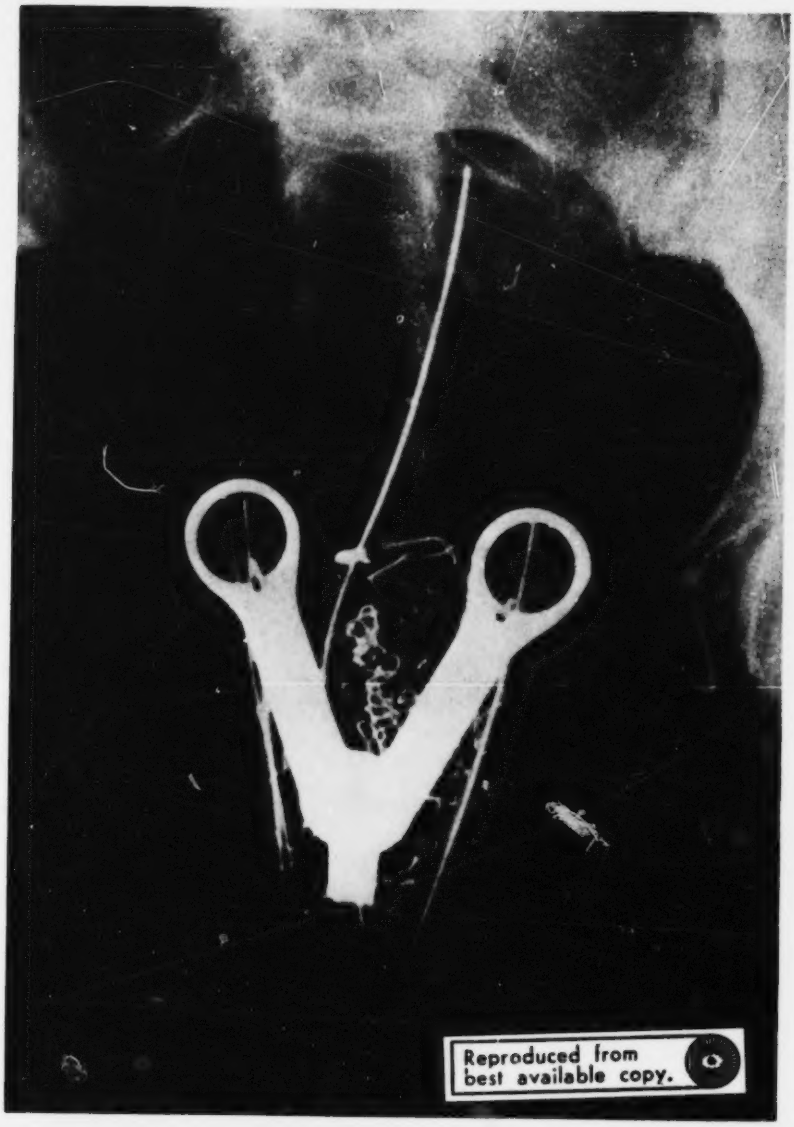

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Figure 4. Silverstone colpostat adapted for afterloading, roentgenogram of pelvis.
T - Afterloaded tandem
C - Afterloaded colpostat

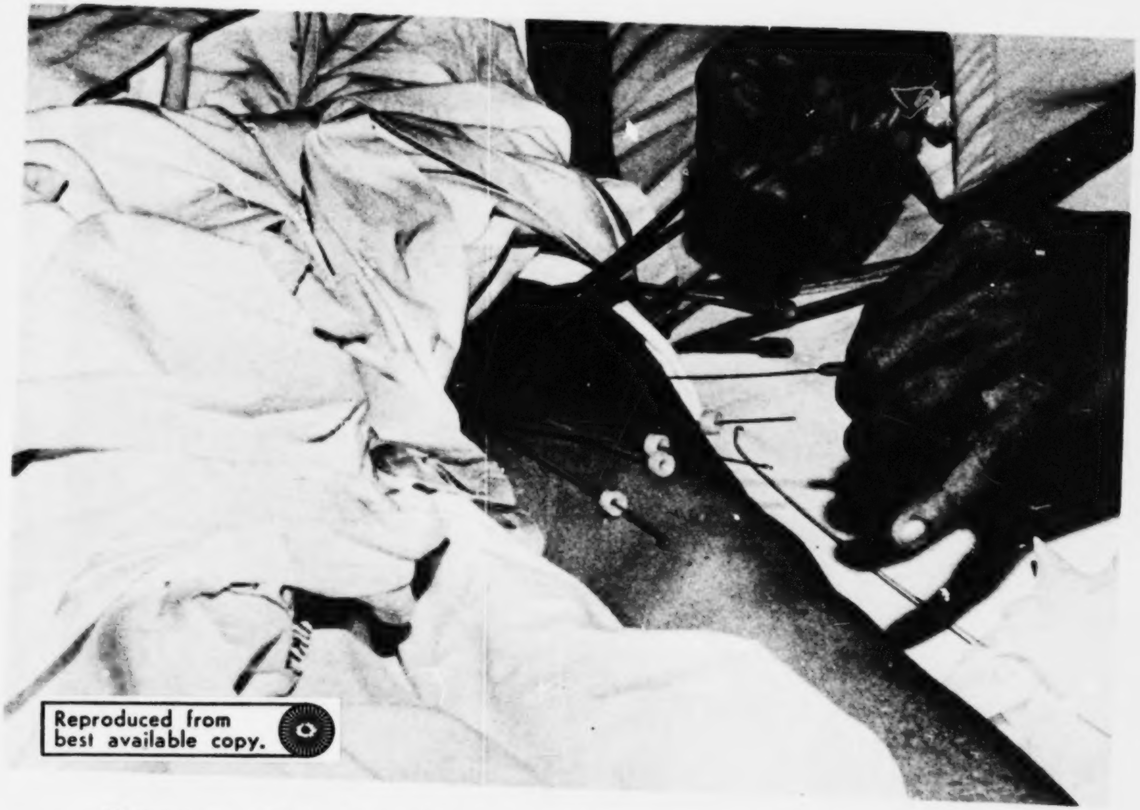

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Figure 5. Technique of afterloading, removal of inactive wires, insertion of cesium 137 wires.

THE BRACHYTRON III

A Remote Afterloader Employing Multiple, Oscillating, High Intensity Sources

Frederick W. George III, M.D., Peter Spiegler, Ph.D.,
George Harwood, B.Sc., Samuel S. Kurohara, M.D., Ph.D.,
Frank Ellis, M.D., and James F. Nolan, M.D.

The Brachytron[1] is a newly developed, high-intensity, multiple-source, remote afterloading brachycurietherapy unit that offers variable position cycling, a unique capability among such devices. It permits the operator to preselect for each source, separately, a range of oscillations varying from 2 to 16 cm, with the sources cycled automatically for variable periods as determined by individual timers. In addition, the position of the center of amplitude in source oscillation can be varied. The cycling makes it possible to simulate linear cobalt 60 sources ranging from 2 to 16 cm in length. Each oscillation sequence can be programmed along a 16 cm range so that different linear intensities are simulated, producing a considerable variety of radiation patterns.

This report is a review of preclinical phase of the USC Brachytron development program, and a summary of the characteristics of the afterloader.

MATERIALS AND METHOD

The USC Brachytron System (figures 1, 2) has two sets of functional elements. The first set, comprising the basic system, consists of:

1. Control console
2. Drive system and unwired flexible cables
3. Source container and source capsules
4. Wired flexible cables and treatment catheters.

---

[1] A similar device is in clinical operation at the University of California (San Diego) Hospital. Both devices were manufactured by AECL.

The second set of elements include:

1. Treatment cave

2. Treatment stretcher dolly and interchangeable stretcher top.

The control console (Brachytron) is a three-panel complex of two identical outer panels, and a center panel with three common controls: the "Key," "Emergency," and "Simultaneous Start" switches. The three digital timer faces are color-coded blue, black, and yellow - a code system that holds for all components associated with any of the three sources. The "Source Position" panel lamp indicates when a source has left the source container, and when it is oscillating.

A "Source Out" switch on each panel initiates treatment (either stationary or cycling) with each source by activating its drive system. The "Hold" switch on each panel temporarily overrides the "Source Out" control, until a "Simultaneous Start" switch on the center panel is activated. (This is when two or more sources are used simultaneously.) An important signal is the "Source Lock/Catheter Secure" light indicating that the base of a treatment catheter has been properly coupled into the system. An auxiliary panel has controls that permit variable centering of the oscillation.

The drive systems are directly behind the console. The treatment room end of the three drive cables are linked to the source capsules on the other side of the wall by screw mechanisms driven by electric motors. Completion of treatment, electrical failure, emergency switch pressure, and several other conditions activate a failsafe system that returns the source capsules to its container.

The source container is a lead-filled, cast steel shell containing three tubes tied together with three source locks. An electrical connection unlocks the source locks and lights color-coded lamps on the treatment catheter end of the source container, as well as on the panels of the control console.

THE TREATMENT CATHETERS AND WIRED FLEXIBLE TUBES

Standard treatment catheters are 10.6 in., teflon-lined, stainless steel tubes -- variously radiused or straight, depending upon clinical need and length of the source capsule. (Larger source capsules require larger radius curves if they are to oscillate safely through the treatment catheters.) When the treatment catheters are properly locked into position, a circuit is completed; this opens the source locks and lights the "Catheters Secure" lamp.

The treatment cave consists of a carpet-covered steel vault with two open ends in the treatment room. The source container is mounted on the roof of the cave. The treatment cave has several purposes:

1. It supplements the room shielding for protective purposes.

2. It reduces radiation to the body of the patient whose extremities are being treated with the Brachytron.

3. In the event of failure of any of the Brachytron source capsules to return to the source container, it makes it possible for personnel to enter the room, activate the source-container return control, disconnect and remove the patient from the device, without exceeding permissible exposure limits.

THE INTERCHANGEABLE-TOP TREATMENT STRETCHER

The treatment couch in the USC Brachytron system consists of a stretcher dolly and a top that is interchangeable with the top of the radiation therapy simulator adjacent to the treatment room. The importance of this component is related to the proper positioning of the intracavitary applicators into which are inserted the treatment catheters. The interchangeable stretcher top is a polyurethane foam mold especially constructed to immobilize and position each patient in the treatment position.

The radiotherapy simulator permits fluoroscopic and radiographic visualization and verification of the position of intracavitary applicators in the precise position in which a patient is to be treated. The interchangeable stretcher top can then be transferred to the treatment cave, and the catheters introduced into the intracavitary applicators, without movement of the patient relative to the stretcher top. The applicators, visualized fluoroscopically and verified radiographically can be maintained precisely throughout the entire treatment.

The patient may be treated in this same polyurethane positioning mold in the teletherapy room where she is given external radiotherapy treatment, so that the intracavitary and teletherapy dosimetry may have a consistent relationship with each other. Substantial changes can occur in the position of the patient's viscera and the intracavitary applicators with changes in the patient's position.

CALIBRATION AND ISODOSE DATA

Figure 3 indicates the dimensions of the sources and the construction of the source capsule. The position of the sources relative to the end of the treatment catheter was investigated by scanning with a probe of the Victoreen Radicon 555 NBS-calibrated for cobalt 60 radiation. The activity in the catheter was demonstrated to occupy an area extending from a point 1.2 cm from the end of the treatment catheter to a point 1.5 cm from the end of the catheter.

Calibration of the sources was also accomplished with the Victoreen Radicon 555 and cobalt 60 probe and yielded the data indicated in table 1.

In order to locate the center of oscillation, the probe was positioned at 2-cm intervals from the end of the catheter. Integrated exposures were measured over 5-minute time intervals. During exposure, the source was allowed to oscillate over 16 cm in the first experiment, and 10 cm in the second. From the data, it is concluded that in doing dosimetry calculations one should use a line source of a length equivalent to the length of oscillation, the center of which is located at a distance 0+2/2 from the end of the catheter, (0 being the length of oscillation).

Experimental determination of the isodose patterns produced by oscillation of the sources to simulate linear cobalt sources of various active lengths was accomplished using film dosimetry. Comparison of the calculated isodose patterns for cobalt 60 sources of linear activities 10 cm and 12.5 cm, with the experimentally derived patterns, revealed them to be virtually identical.

These findings indicate that calculated isodose curves can be used to predict dose distributions in clinical applications.

CLINICAL DOSIMETRY AND TREATMENT PLANNING

The biologic dosimetric problems associated with the use of high-intensity sources for intracavitary therapy have been recognized as considerably more perplexing than the physical dosimetric aspects described above.

A remote afterloader with source cycling capability at the Memorial Center for Cancer and Allied Diseases has been used experimentally in patients with cancer of the cervix, endometrium, and other sites. A commercially available high intensity remote afterloader (the Cathetron) is in use at Charing Cross, Cardiff, Birmingham, and three other radiotherapy centers in Great Britain. In Japan, M. Wakabayashi, at the University of Hok-Kaido has used the Ralstron, a high-intensity remote afterloading device since 1968. The sister unit of the USC Brachytron is in use at UCSD. There are no other high-intensity afterloaders known to the authors.

The experience of these workers with high-intensity remote afterloading in the treatment of cancer of the cervix has been studied in the development of optimal treatment regimens with the Brachytron, since the point A dose rates of the Cathetron (about 200 rads/min - Joslin) and the Ralstron (500 rads/min) are comparable to that of the Brachytron (200 rads/min). Existing USC radiation regimens used in intracavitary curietherapy for cancer of the cervix were analyzed to establish the nominal single dose expressed at point A for comparison with those of other clinics employing high-intensity afterloading. A tabulation of the USC radiation regimens for various stages of cervix carcinoma and the calculated biological equivalent doses in rets is presented in table 2.

As this tabulation indicates, the USC nominal single dose in rets for cervix cancer patients assessed at point A is 2,600 rets. The biologic dose associated with the regimen of high-intensity pelvic intracavitary curietherapy plus external therapy, which Joslin employs, is calculated to be approximately 2,550 rets. Two conventional low-intensity techniques, also employed by Joslin prior to his initiating his cathetron regimen, were calculated to produce NSD values of 2,590 and 2,430 rets -- about the same (table 2) as the NSD here at the LAC-USC Medical Center. The biological reactions associated with Joslin high-intensity afterloading regimen and the two conventional low-intensity regimens were similar. Since nominal single doses are similar, as are dose rates to point A of the Brachytron and Cathetron it seems reasonable to consider using Joslin's cervix regimen with the Brachytron. This regimen consists of 3,900 Cathetron rads in four fractions (975 rads/fraction) in 21 days, with 2,400 rads from telecobalt in 12 fractions concurrently.

Wakabayashi has reported that fractionation regimens producing point A doses of 2,000 or 1,460 rads given in a single treatment, concurrent with hyperbaric therapy, resulted in adequate clinical responses. By contrast, 752 or 660 rads in three fractions in 2 weeks did not produce adequate clinical reactions. Since this high dose rate experience was associated with concurrent hyperbaric therapy, it is of limited value in developing normobaric high-intensity regimens.

Further investigation of time-dose fractionation has included developing a modification of the Ellis formula for use in converting nominal single doses to point A doses.

Several fractionation regimens based on 2,500 rets NSD are listed in table 3. These therapeutic regimens are for Stage I patients in whom no concurrent external radiotherapy would be employed. In addition, a table for converting rads to rets for various number of treatment sessions and times has been devised (table 4).

A preliminary working method for simple point A dosimetry in Brachytron patients has been developed in the form of a dosimetry program. This program runs on the Wang 700 programable calculator, and calculates doses to point A or any other point from one or more of the sources as point or line (oscillating) sources.

DISCUSSION

At the LAC-USC Medical Center, Fletcher-Suit hand afterloading techniques are employed in about eight patients per week in the routine intracavitary therapy of gynecologic malignancies. Radiation exposure problems to physicians in the operating room have been virtually eliminated by manual afterloading techniques, but radiation exposure to nurses and aides in the radiotherapy ward remain a constant problem. This problem has grown steadily more acute due to increasing employment of interstitial implants in patients who are housed with or near intracavitary patients. LVN and nursing personnel in the radiotherapy ward have approached maximal permitted levels of radiation exposure with the increasing patient load, requiring a cutback in the utilization of brachycurietherapy.

Incorporation of the Brachytron III Remote Afterloader into a clinical radiotherapy system offers solutions to these problems, as well as certain other important advantages. These include:

1. Option of setting up patients and visualizing the intracavitary applicators fluoroscopically and radiographically in the treatment position.
2. Opportunity to position and immobilize patients on a polyurethane foam mold interchangeable stretcher top on the simulator, and thereafter without changing the patient's position to transfer patient and stretcher top to the Brachytron treatment room.
3. Ability to carry out treatments in a shielded cave with no exposure to other personnel or patients, and no transport of radioactive materials outside the room.
4. Capability of completing an intracavitary radiation treatment in 10 minutes or less while the patient is completely immobilized and continuously monitored, eliminating the likelihood of movement of the sources associated with conventional techniques.
5. Elimination of long periods of immobilization in bed (hazardous in patients with cardiovascular disease or respiratory disease, and any older patient).
6. Capacity to treat many different patients during a week's time without requiring large stockpiles of radionuclides and elaborate storage handling facilities.

7. Freeing of radiotherapy beds, not required for intracavitary patients treated on the Brachytron.

8. Ability to simulate a wide range of radiation sources by varying the centering and range of oscillation of point sources, offering better dose distributions in existing applications, since isodose patterns can be tailored to the patient's disease. This also implies increasing the scope of Brachycurietherapy and development of a wide range of new applications, including extending it to the treatment of cancer of the bladder, prostate, rectum, esophagus, and many other superficial and deep tumor sites.

9. Potential for upgrading and modifying the unit to permit computer-assisted control of intracavitary and interstitial treatment, associated dosimetry, and data recording, and to integrate it into the departmental radiotherapy system.

SUMMARY AND CONCLUSIONS

Shielding arrangements, calibration, and isodose curve production have been accomplished for a prototype remote afterloader that features variable amplitude oscillation of multiple high-intensity sources. Mechanical jigs, catheters, and other devices have been developed to facilitate its use in a clinical setting. Clinically effective and tolerable time dose programs have been devised for use with the unit, based on clinical experiences with similar high dose rates elsewhere, and regimens currently in use with conventional afterloading at USC. Appropriate health surveys and operational testing have been accomplished and documented.

This equipment and similar devices may well broaden the scope and upgrade the quality of intracavitary curietherapy, in addition to reducing radiation hazards to personnel and other patients.

Table 1. Source calibration

Source	Activity in Curies[a]
Yellow	3.42
Blue	3.72
Black	4.06

[a] Source activities of 4.0 had been requested

Table 2. Cervix cancer point A RAD and RET doses with USC radiation regimens

Stage	Intra-cavitary (rads)	External beam (rads)	Total (rads)	Total (rets)
I Small	9,000	---	9,000	2,400
I Large & IIA	8,000	2,000	10,000	2,500
IIB Large & IIIA	6,000	4,000	10,000	2,500
IIIB Large & IVA	5,000- 6,000	5,000	10,000- 11,000	2,500- 2,600

Table 3. Point A RAD dose increment to achieve 2,500 RETS

Increments	Days between increments	RADS
1	0	2,111
2	7	1,733
3	14	1,374
4	21	1,155
5	28	1,006

Table 4. RAD to RET conversion table[a]

Number of sessions	Interval between sessions (weeks)			
	1	2	3	4
2	1.463	1.579	1.651	1.704
3	1.740	1.878	1.964	2.027
4	1.950	2.104	2.199	2.271
5	2.123	2.291	2.400	2.473
6	2.273	2.453	2.565	2.647

[a] Multiply required NSD X factor/sessions

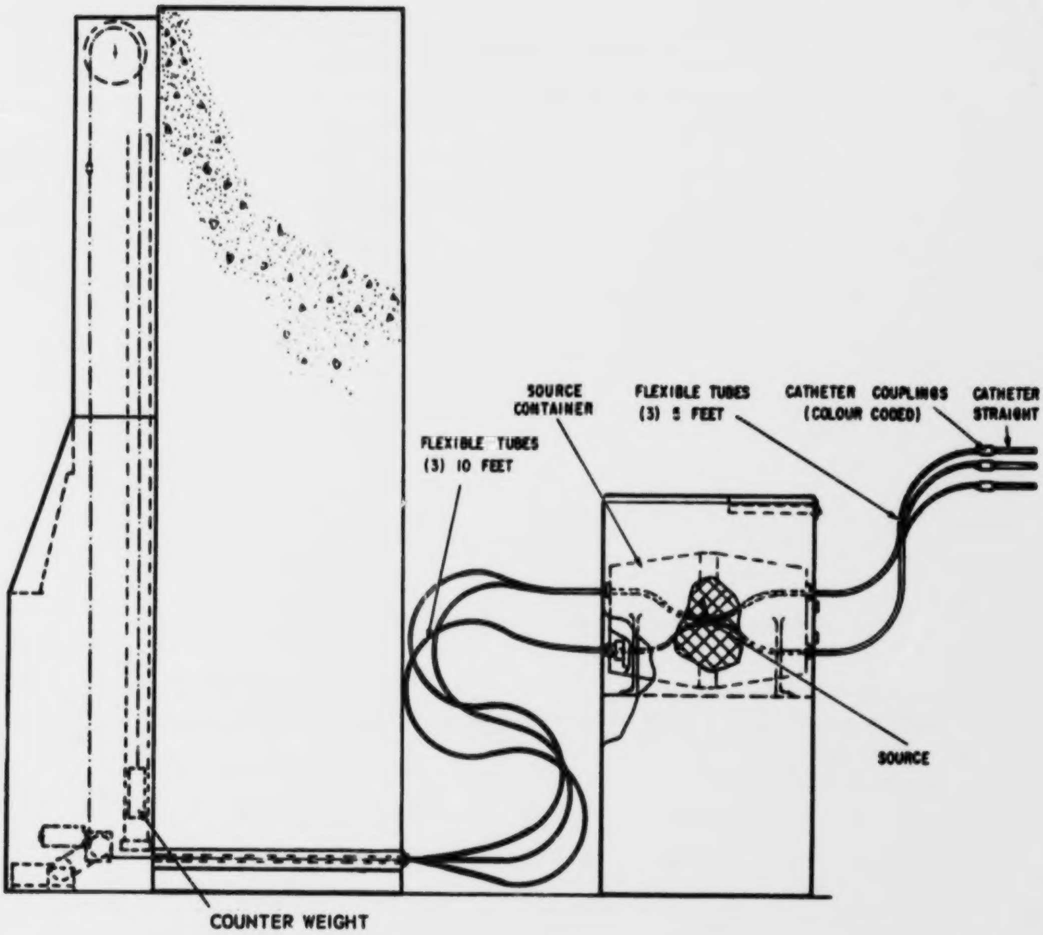

SOURCE CONTAINER
FLEXIBLE TUBES (3) 5 FEET
CATHETER COUPLINGS (COLOUR CODED)
CATHETER STRAIGHT
FLEXIBLE TUBES (3) 10 FEET
SOURCE
COUNTER WEIGHT

Figure 1. Schematic drawing of the Brachytron system.

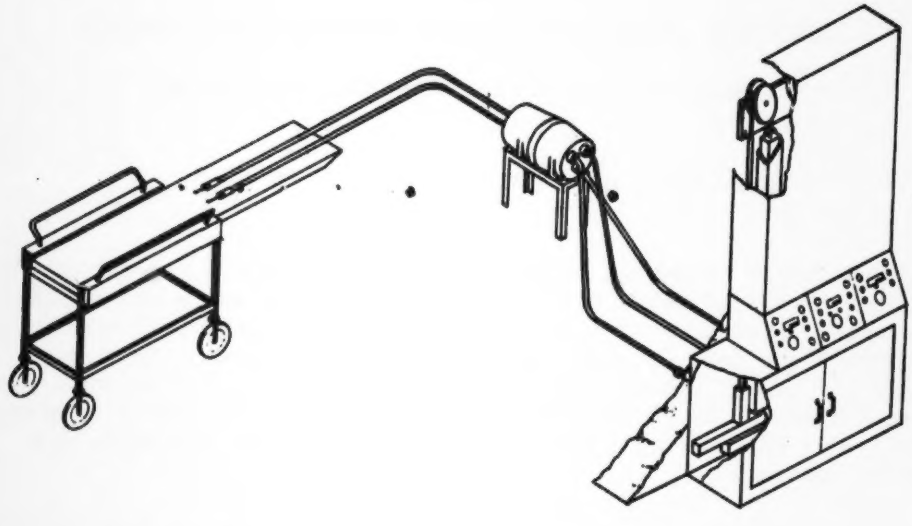
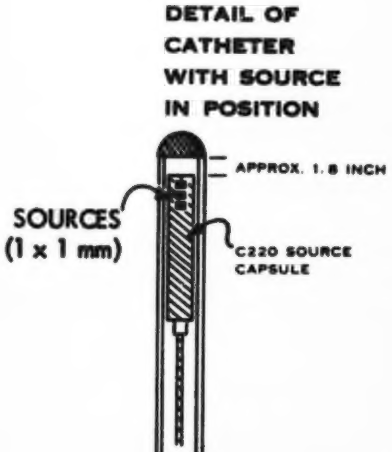


Figure 2. Another view of the Brachytron system.



DETAIL OF CATHETER WITH SOURCE IN POSITION
APPROX. 1.8 INCH
SOURCES (1 x 1 mm)
C220 SOURCE CAPSULE

Figure 3. Detail of catheter, with source in position.

DISPOSABLE AFTERLOADING RADIUM APPLICATOR FOR TREATING CANCER OF THE CERVIX (SUDA-CHARY APPLICATOR)

A. Sudarsanam, M.D. & Komanduri K. N. Charyulu, M.D.

Our desire to design another radium applicator for carcinoma of the cervix was prompted by inadequacies existing among the devices introduced from time to time. Although some of the applicators have withstood the test of time, several problems persist. Some are bulky and heavy, others are difficult to maintain in position. Patients have had to be confined to bed with limited freedom of movement. Our radium applicator was designed with the following distinct features:

1. Capability of constant radium dose distribution to tissue because of a fixed relationship between uterine and vaginal radium and the pelvic tissues
2. Facility for individual therapy planning
3. Easy x-ray visualization
4. Total weight not more than 4 ounces
5. Elimination of vaginal packing, permitting flow of vaginal discharges and minimizing chances of infection
6. Afterloading capability
7. Comfort to patients through (a) freedom to turn around or be propped up in bed; and (b) facility of limited ambulation to suitable patients without fear of ejecting or dislocating the applicator
8. Inexpensive and disposability
9. Capability of predetermined dosimetry, manual or computerized

MATERIALS AND METHODS

Plastic devices are light and lend themselves to mass production; hence, plastics were used for our applicator.

Our earliest model was designed to afterload the vaginal radium sources so that their axes would be perpendicular to the long axis of the vagina, as required by Manchester system. The device was bulky, hence its use was limited to only a few patients.

We then looked at the computerized dosimetry of radium sources in two positions: (1) the classical pattern described by the Manchester system, in which the vaginal sources are perpendicular to the long axis of the vagina; and (2) the pattern where the vaginal sources lie parallel to the long axis of the vagina, as in our system. A higher dose to the rectal and bladder walls, possible in such a position, could be minimized by the use of oblong ovoids in each fornix. Computer printouts of isodoses for the two positions (figures 1-8) enabled us to design the applicator described. The main parts of the appliance are:

(a) Two plastic ovoids connected to plastic forniceal tubes. Plastic cups can be used over the ovoids to provide increased separation where the pelvis and vagina are wide and roomy. Four types of forniceal tubes are available; (1) straight or with outward bend, (2) 5°, (3) 7 1/2°, and (4) 10°. The angulation will permit assorted separations between the ovoids. The forniceal tubes have flat grooves that fit into the jaws of the clamp and prevent rotation of the ovoids when affixed in position. Different lengths of forniceal tubes are available to suit the length of the vagina.

(b) A central thin-wall, stainless steel uterine tube graduated in inches. The tube can be bent in the operating room to provide a gentle curve to suit the length of the uterine canal. An "O" rubber ring presents the length of insertion into the uterus. A short length of rubber tubing is mounted at the outer end to facilitate fixation in position.

(c) A plastic clamp with two jaws. The clamp holds the tubes in position by clamping them outside the vulva. The jaws are tightened over the tubes by bolts with wing nuts. When tightened, the radium applicator assumes the predetermined pattern.

(d) A waist leather belt that attaches to the clamp anteriorly and posteriorly by fabric tape (hernia tape). Four holes are provided at each corner of the clamp.

The applicator and the individual parts are shown in figures 9 and 10.

Preplanning of therapy is possible with the system. The width available at the vaginal vault is determined by a pelvimeter[1] shown in figure 11. The width of the vault and the disposition of cancer helps to select the appropriate forniceal tube.

PROCEDURE

Opaque markers such as inactive radon seeds are inserted into the lips of the cervix and the lower edge of disease in the vaginal wall, under general anesthesia or paracervical block. A Foley catheter is left in place.

When the cervix has been dilated the uterine tube is introduced. The two forniceal tubes, curving outward, are slipped in one at a time, so that the ovoids lie in each fornix. The clamp is affixed over the three tubes and the jaws are tightened. The forniceal tubes can be manipulated into final position as the grooves over the tube slip into their proper place. The applicator clamp is fastened to the belt anteriorly and posteriorly, using fabric tape, and protective pads are slipped under the tape to prevent excoriation of the groin. Packing the vagina is unnecessary (figure 12).

Dummy radium sources in plastic inserts in the forniceal and uterine tubes permit x-ray localization. Selection of the number of radium sources and their quantity is based on the localization films. Coplanar, AP and crosstable lateral x-ray films and magnification ring in vagina are used in accurate computer dosimetry (figures 13-16).

The appropriate radium sources then are inserted and held in place by a small length of adhesive tape.

Rectal and bladder dosimetry are carried out with a Mauderli probe.

RESULTS

Some 28 patients have been treated with the applicator.

Although the device permits any radium load, on an average, three sources were used in uterine tandem: a proximal 15 mg and two 10 mg sources. The ovoids each contained 15 mg sources. When the pelvis was roomy, 20 mg sources were used in the ovoids. The radium was left in place for 77 hours to give 5,000 mg hours, the existing practice. When the 20 mg sources were used, the computer dosimetry governed the length of radium application. Where disease was present over the lower portion of the vagina, individual patients were given additional radium. Our patients previously received 3,300 rads in 4 weeks for Stages I and II, 3,850 rads in 4 weeks in Stage III and selected cases of Stage IV of external teletherapy.

---

[1] Available from Radium Chemical Company, New York.

The rectal dose as measured by the Mauderli probe varied from 30 R/hr to 40 R/hr over a short length of the anterior rectal wall. No complications have been seen. The longest followup has been over 1 1/2 years.

Check x rays with applicator in place were made of patients in various positions such as lying on the side, standing, and resuming the recumbent position. Serial x rays on various days after insertion were also taken. No displacement of the radium system with respect to the pelvic structures was noted.

DISCUSSION

The applicator described permits individualized therapy of patients with carcinoma of the cervix. It has distinct features previously mentioned. The applicator could, perhaps, be used in conjunction with cathetron, as the uterine and forniceal tubes simply would serve as guides.

Several patients in good general condition have found it an advantage to have limited ambulation under supervision. Certain precautions are necessary if ambulation is allowed. However, we would not advocate ambulation of aged and weak patients, as they are likely to be unsteady on their feet. It was also an advantage to patients to be able to turn around in bed, or be propped up to eat.

No discomfort was associated with the applicator on the second day. Absence of vaginal packing helps the vaginal discharge to flow out; foul odor and infections associated with radium applications thus are eliminated. Radium application is more effective in the absence of infection.

It is hoped that a computerized set of isodoses will be available for all permutations and combinations possible with the applicator. If so, the isodoses can simply be superimposed on the check films, taking magnification into account.

The applicator permits asymmetric assembly when one fornix is filled with tumor. It retains the advantages of some of the systems that have been hitherto designed, while introducing flexibility and individualization.

SUMMARY

A simple afterloading, disposable radium applicator for carcinoma of the cervix has been described. In our experience, we find it more useful than appplicators currently available.

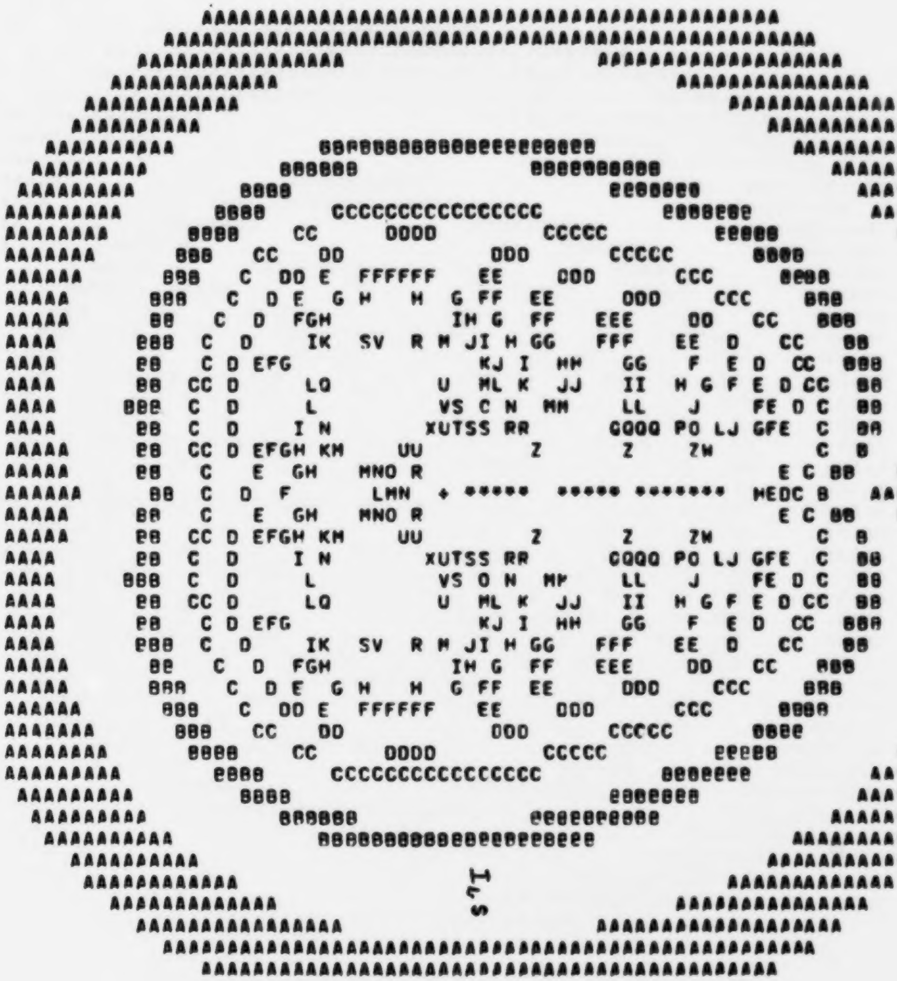


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Figure 1. Isodose printout - 15, 10, 10 mg uterine tandem and 15 mg in each fornix, Manchester method. Ideal case - Sagittal plane of radium system.

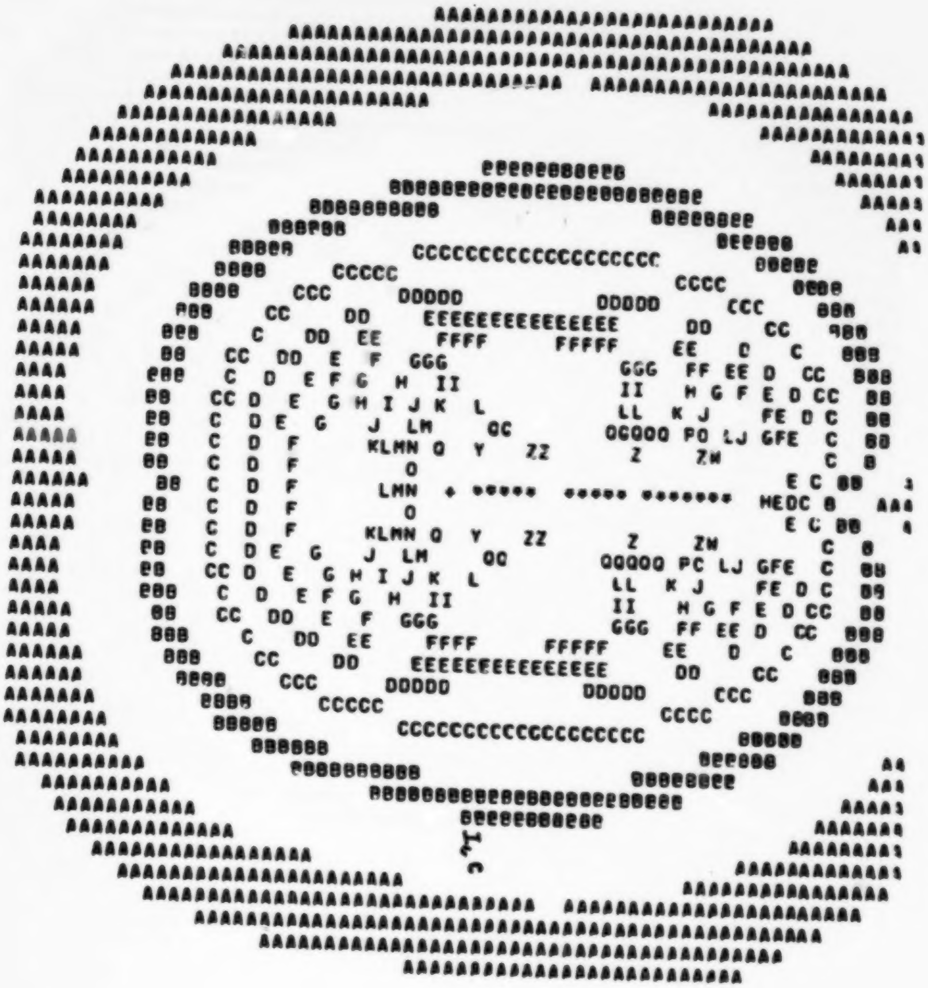

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Figure 2. Isodose printout - 15, 10, 10 mg uterine tandem and 15 mg in each fornix, Manchester method. Ideal case - Coronal plane of pelvis.

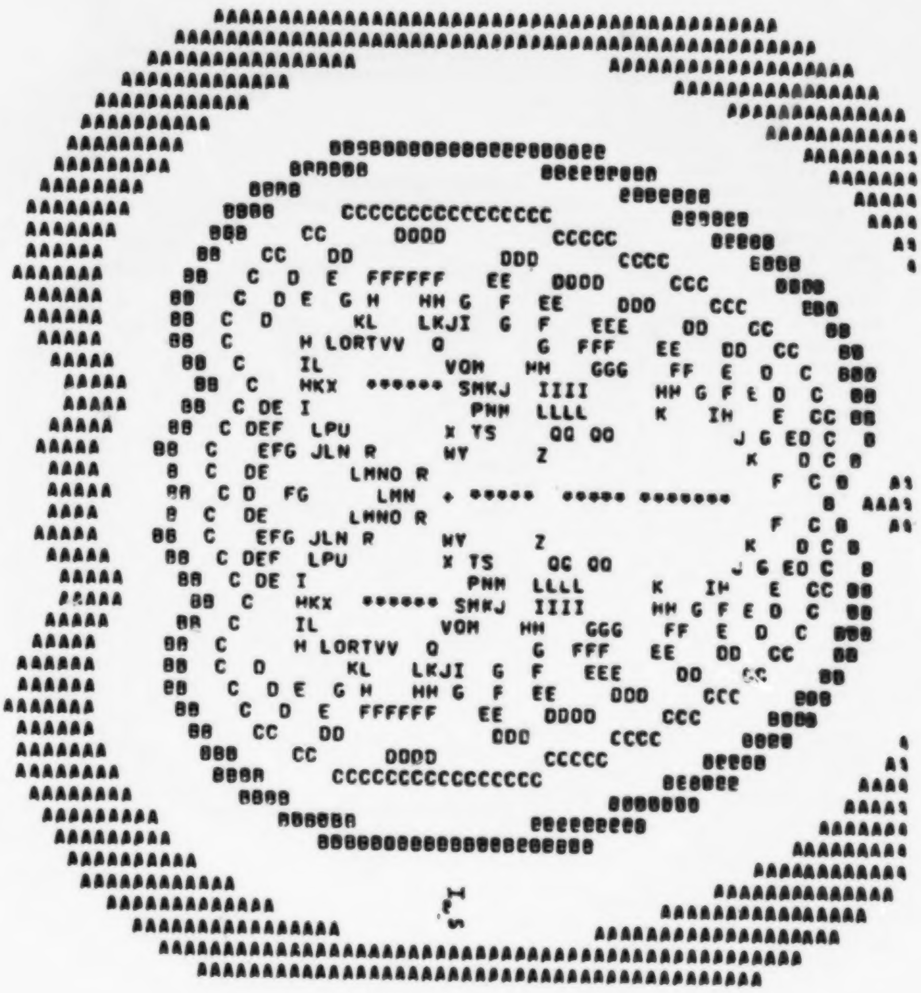

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Figure 3. Isodose printout - 15, 10, 10 mg uterine tandem, 15 mg in each fornix with axes of sources parallel to vaginal axis. Ideal case - Sagittal plane of radium system.

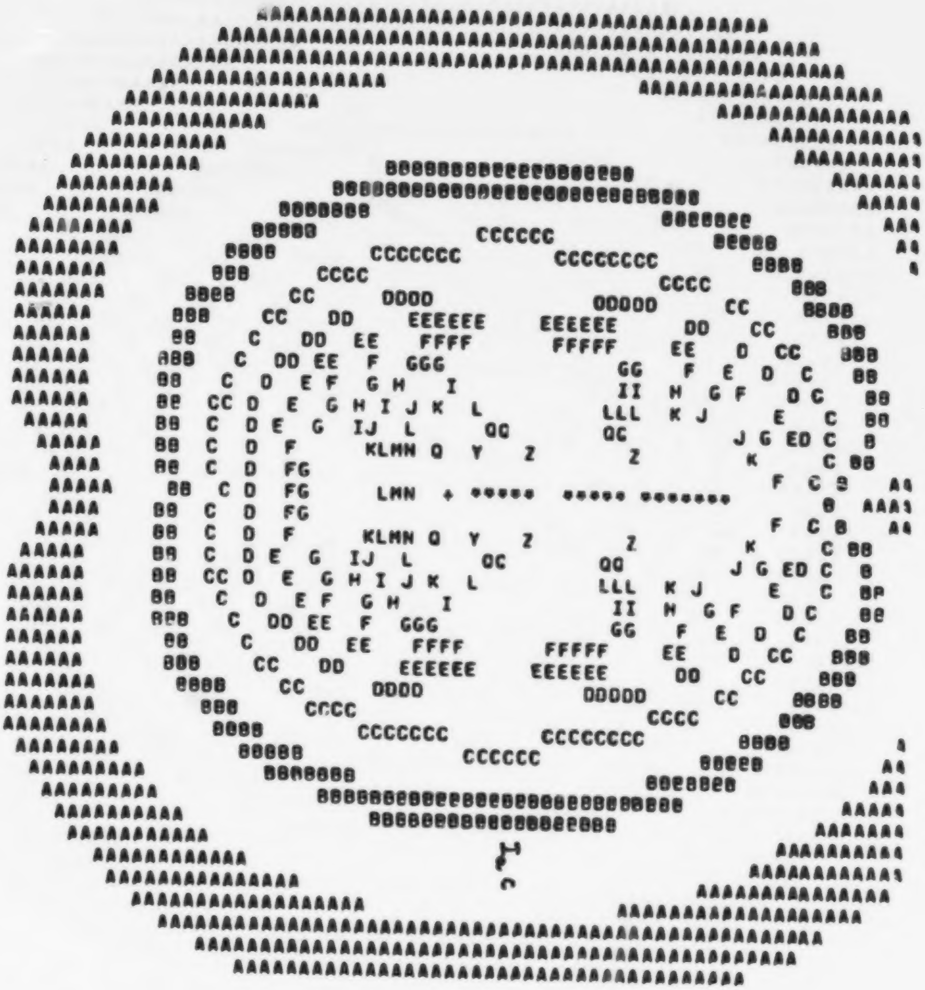

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Figure 4. Isodose printout - 15, 10, 10 mg uterine tandem, 15 mg in each fornix with axes of sources parallel to vaginal axis. Ideal case - Coronal plane.

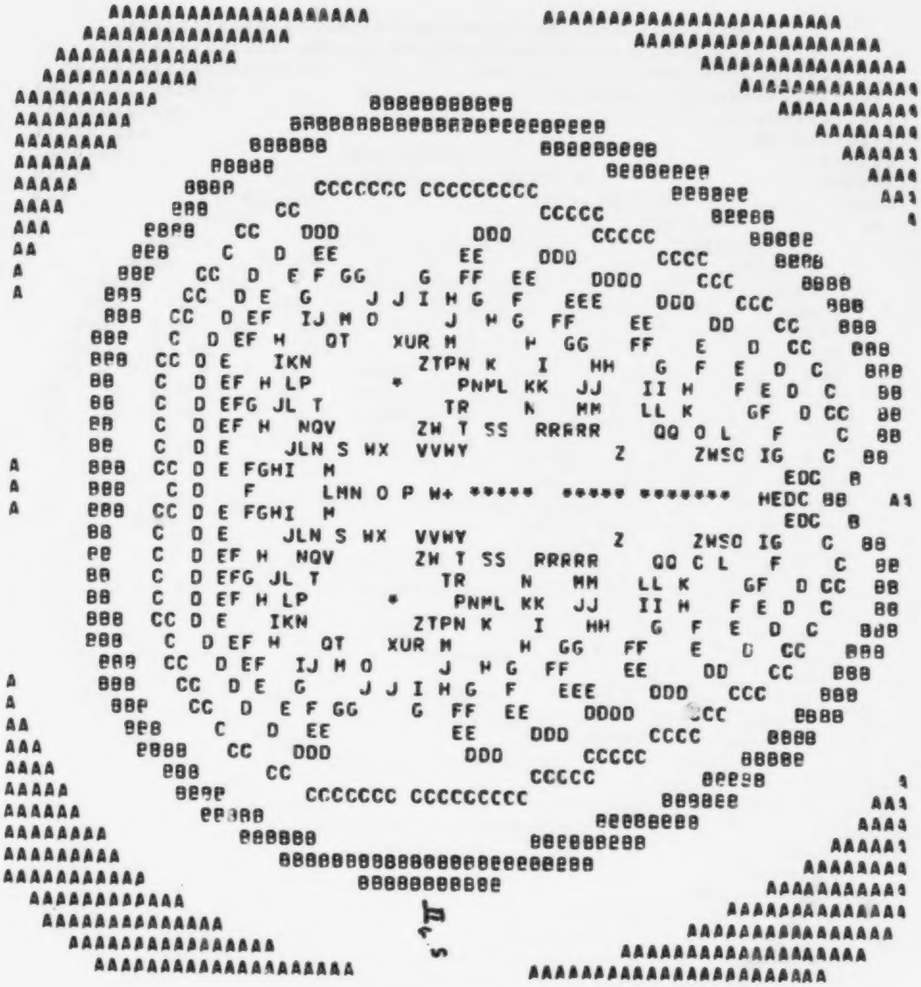

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Figure 5. Isodose printout - 15, 10, 10 mg uterine tandem and 20 mg in each fornix, Manchester method. Ideal case - Sagittal plane of radium system.

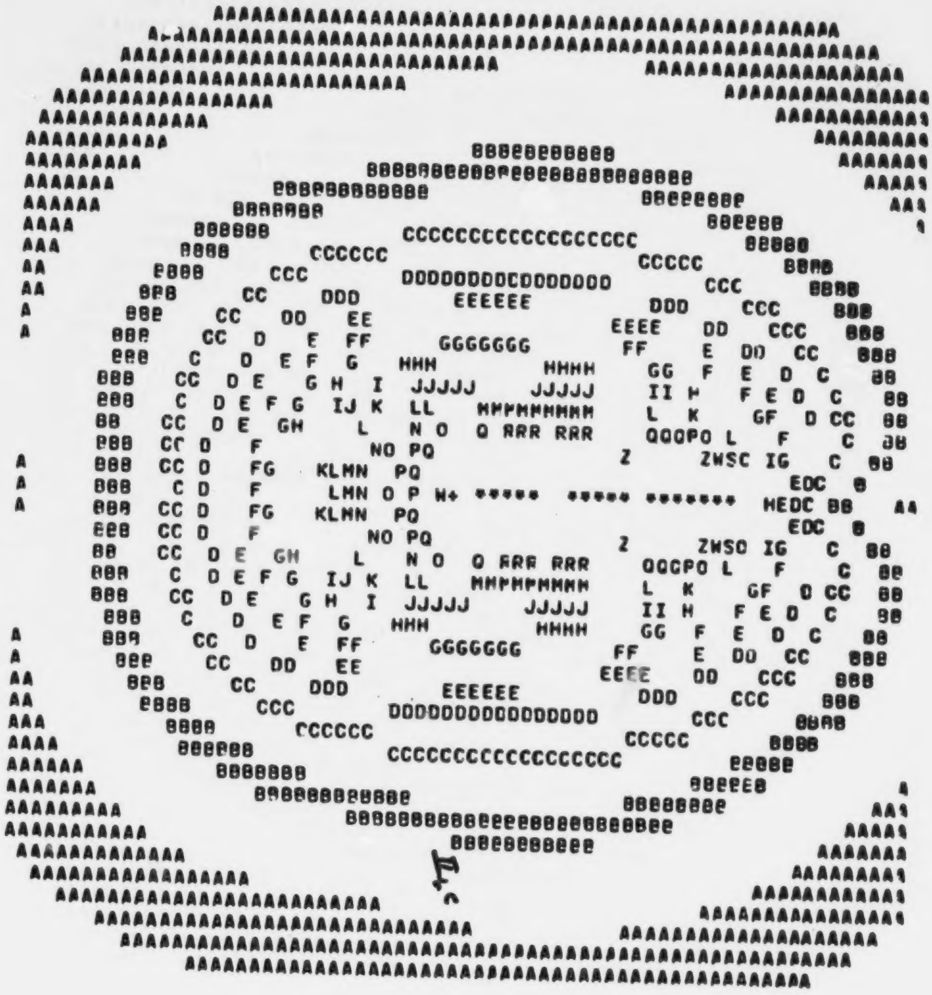

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Figure 6. Isodose printout - 15, 10, 10 mg uterine tandem and 20 mg in each fornix, Manchester method. Ideal case - Coronal plane of pelvis.

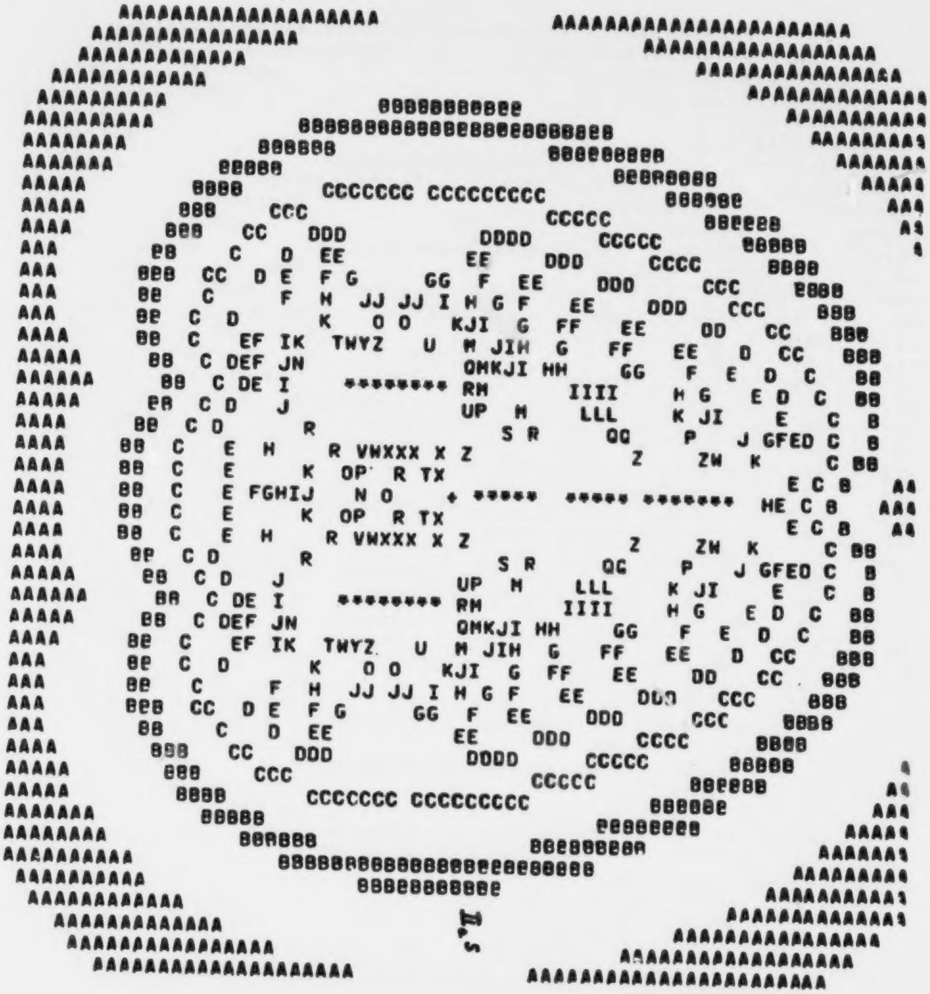

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Figure 7. Isodose printout - 15, 10, 10 mg uterine tandem and 20 mg in each fornix with axes of sources parallel to vaginal axis. Ideal case - Sagittal plane of radium system.

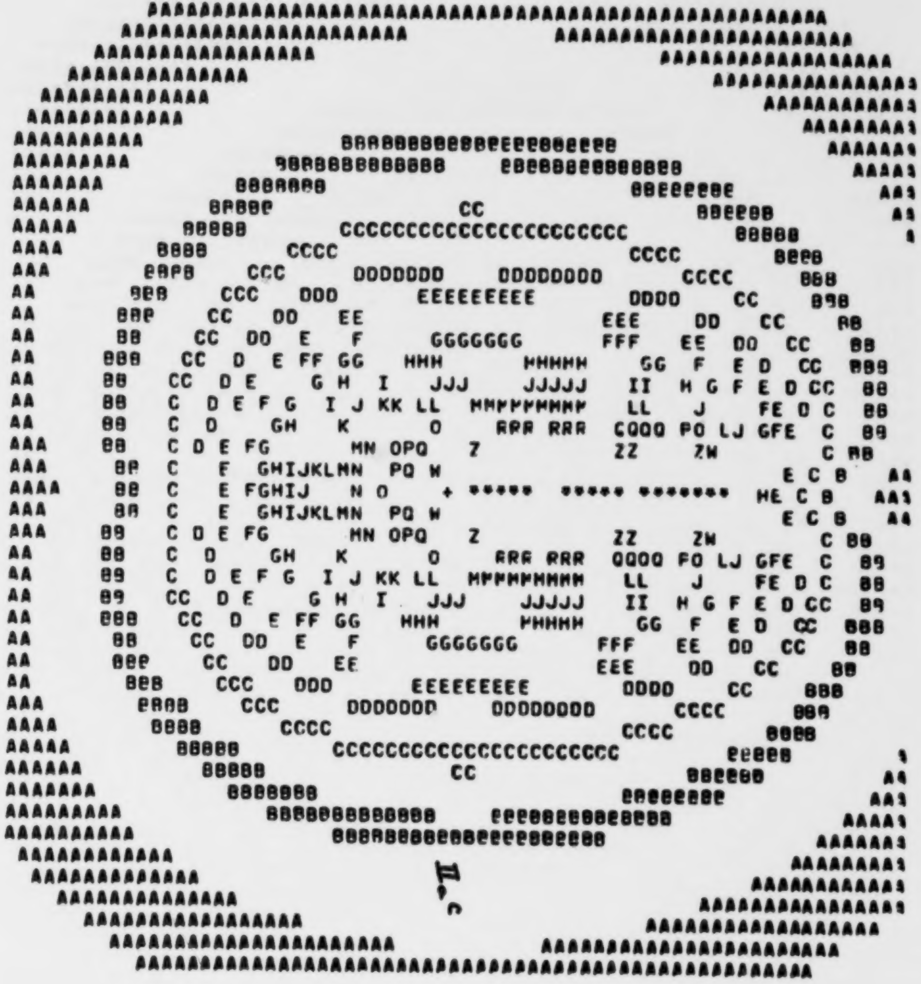

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Figure 8. Isodose printout - 15, 10, 10 mg uterine tandem and 20 mg in each fornix with axes of sources parallel to vaginal axis. Ideal case - Coronal plane of pelvis.

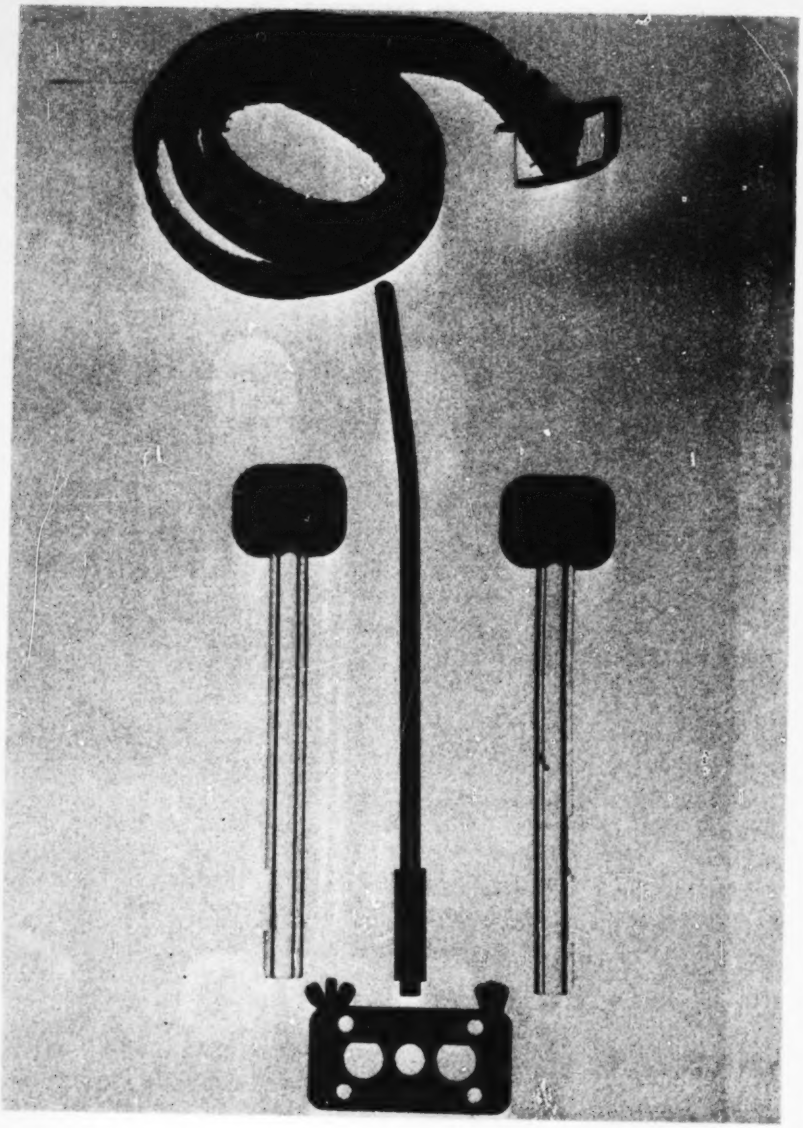

Figure 9. Parts of applicator.

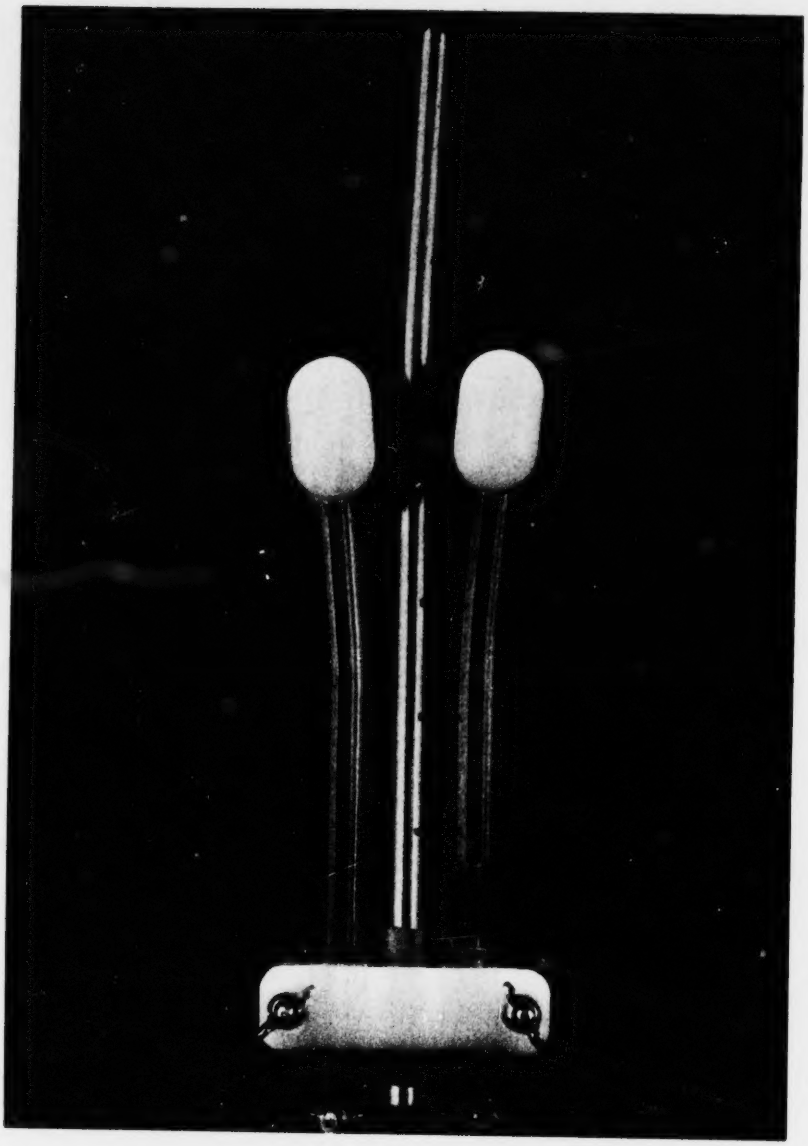

Figure 10a. Applicator when assembled.

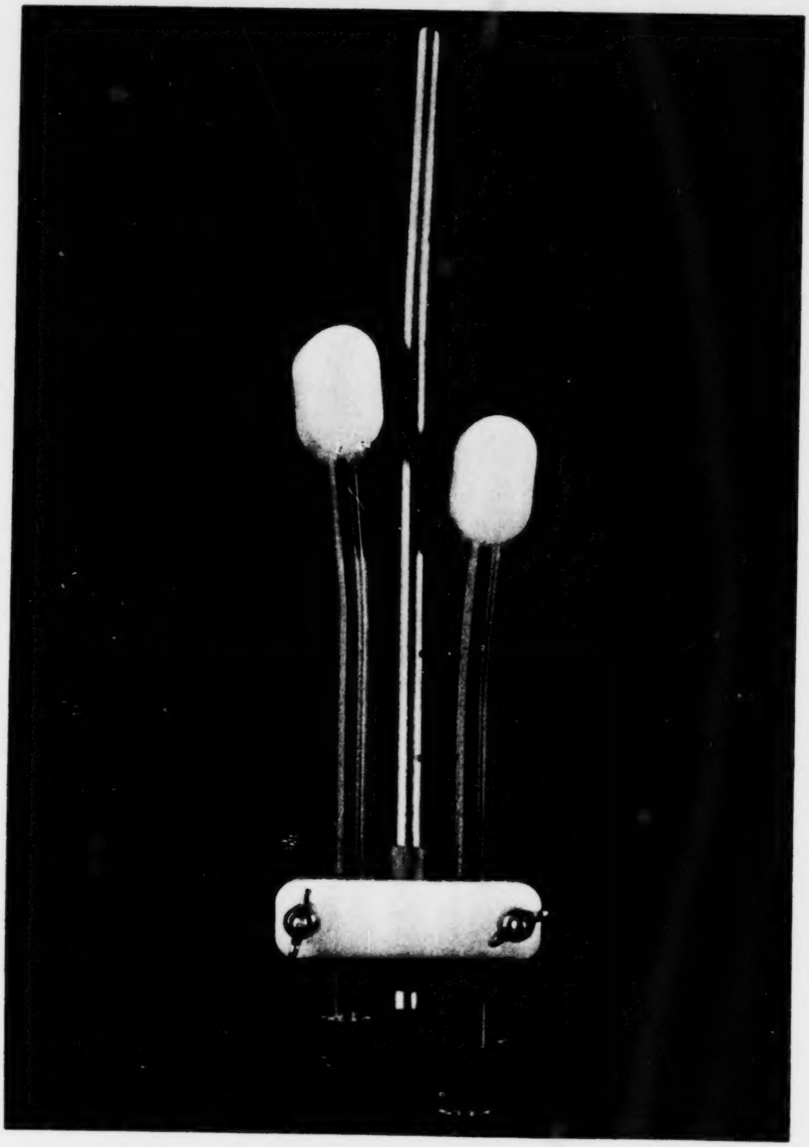

Figure 10b. Applicator when assembled.

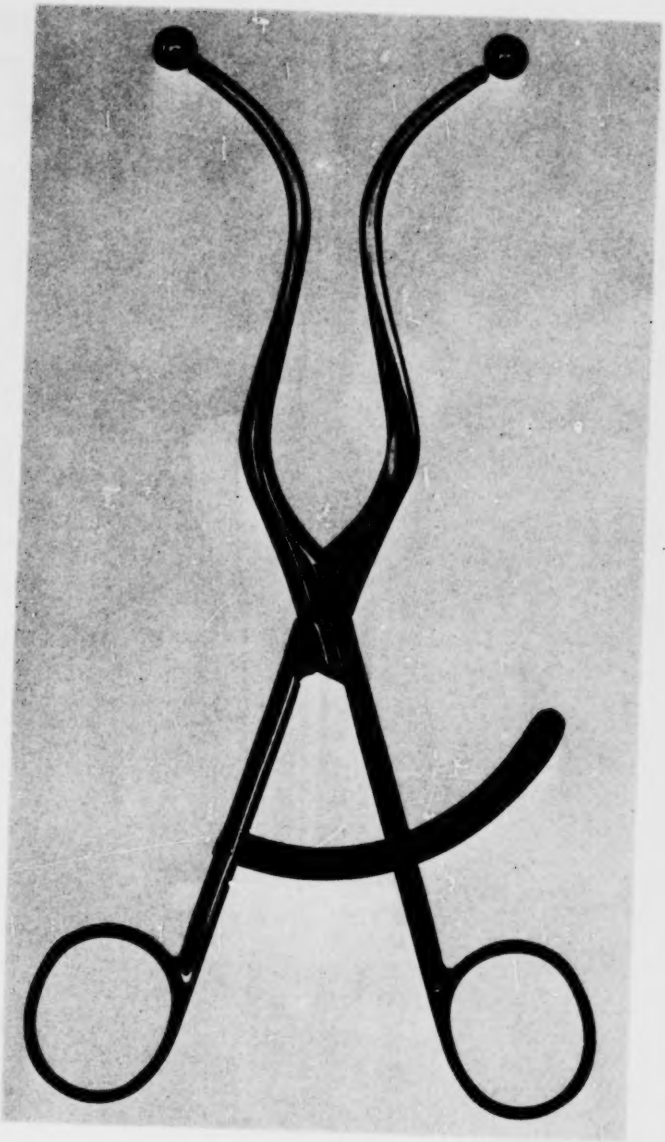

Figure 11. Pelvimeter.

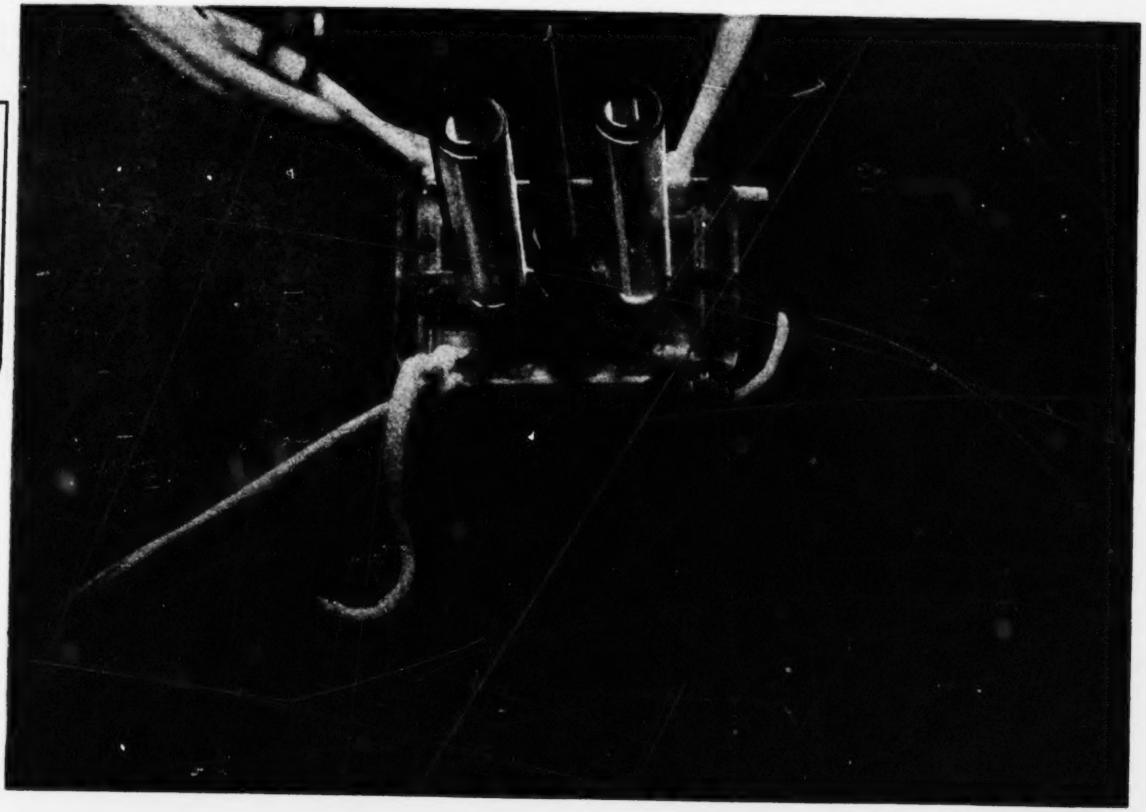

Figure 12. Photo of applicator in position in patient.
Protective pads in groins yet to be inserted.

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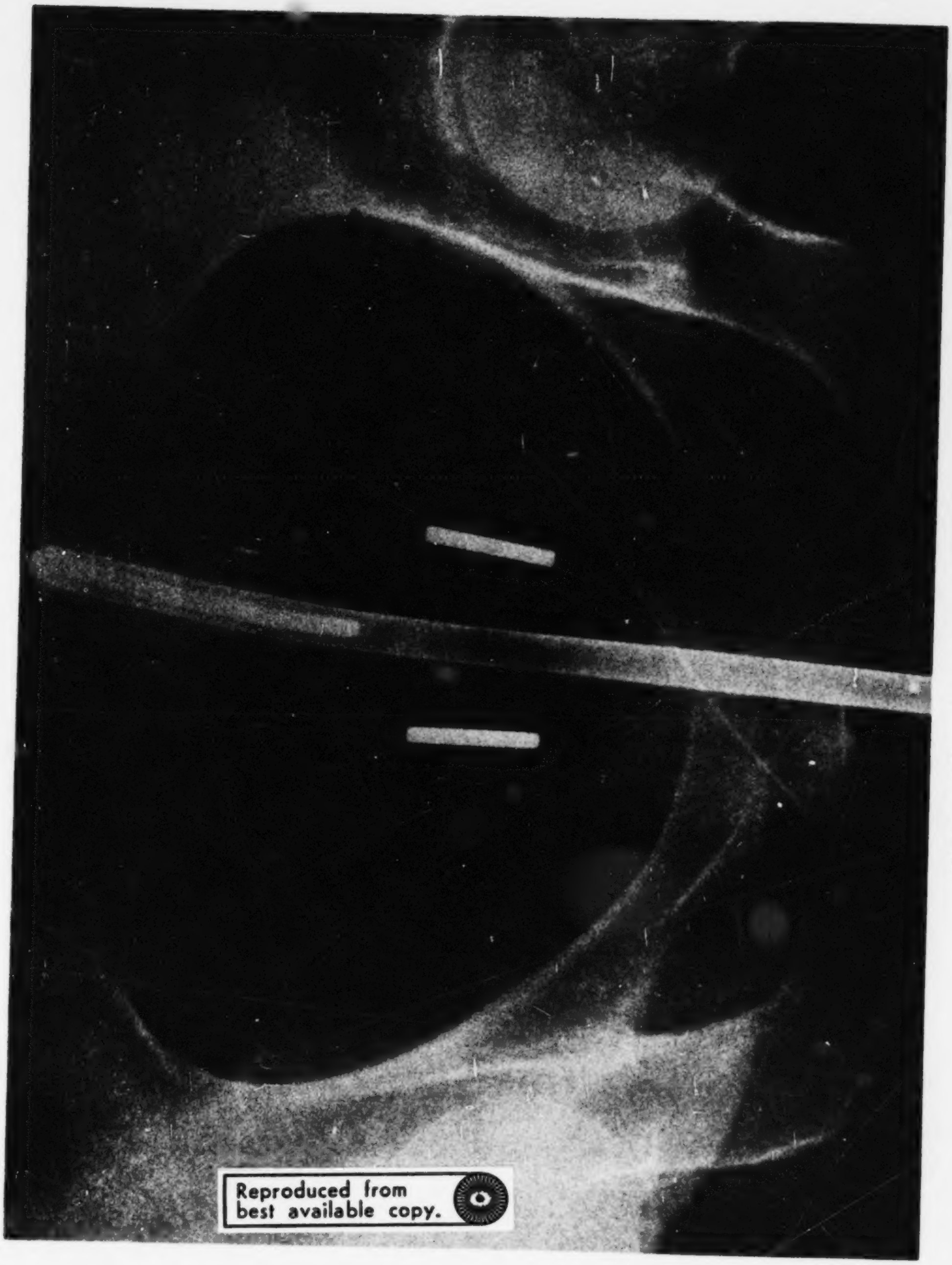

Figure 13. Localization radipgraph, AP.

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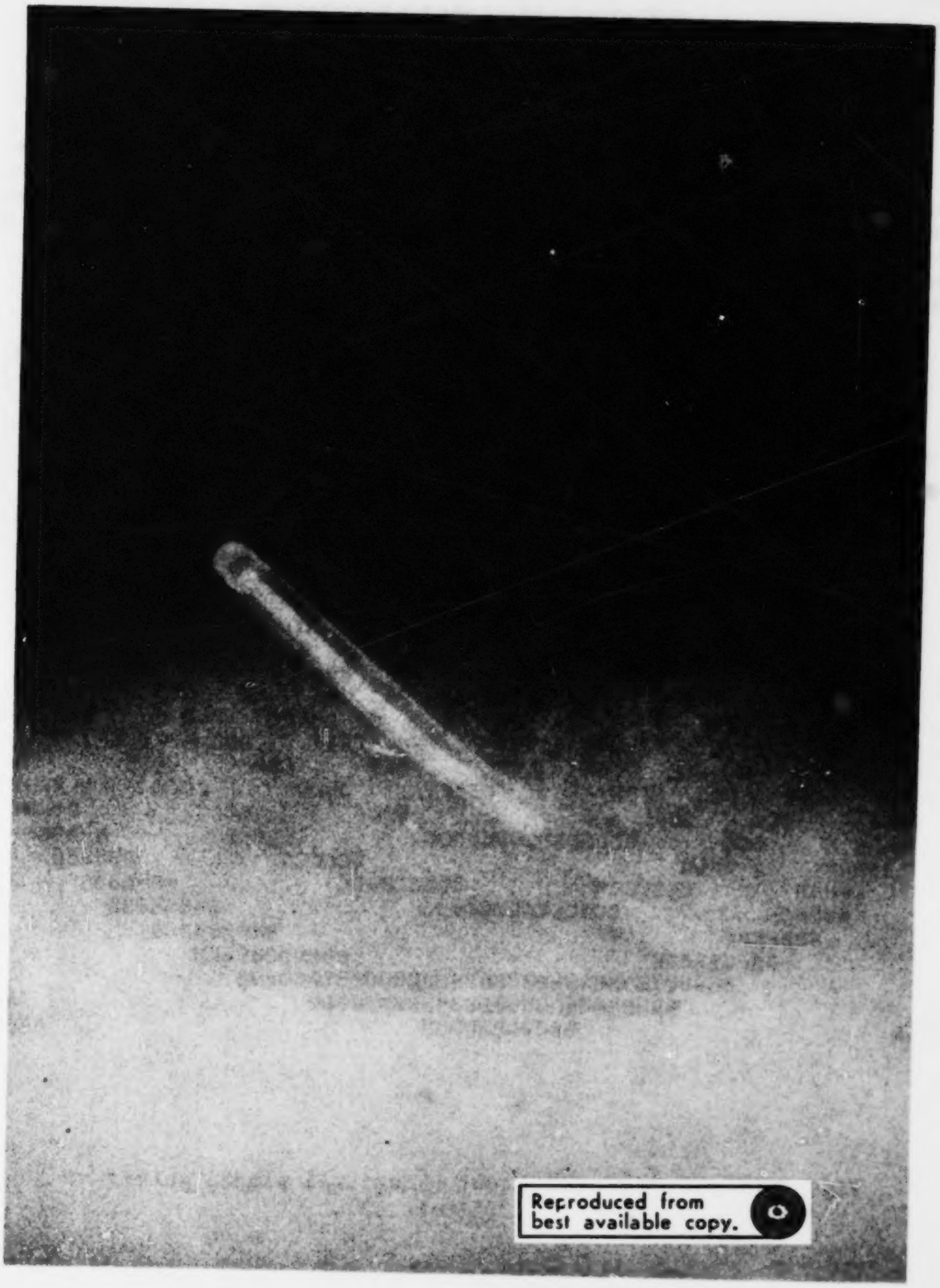

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Figure 14. Localization radiograph, lateral.

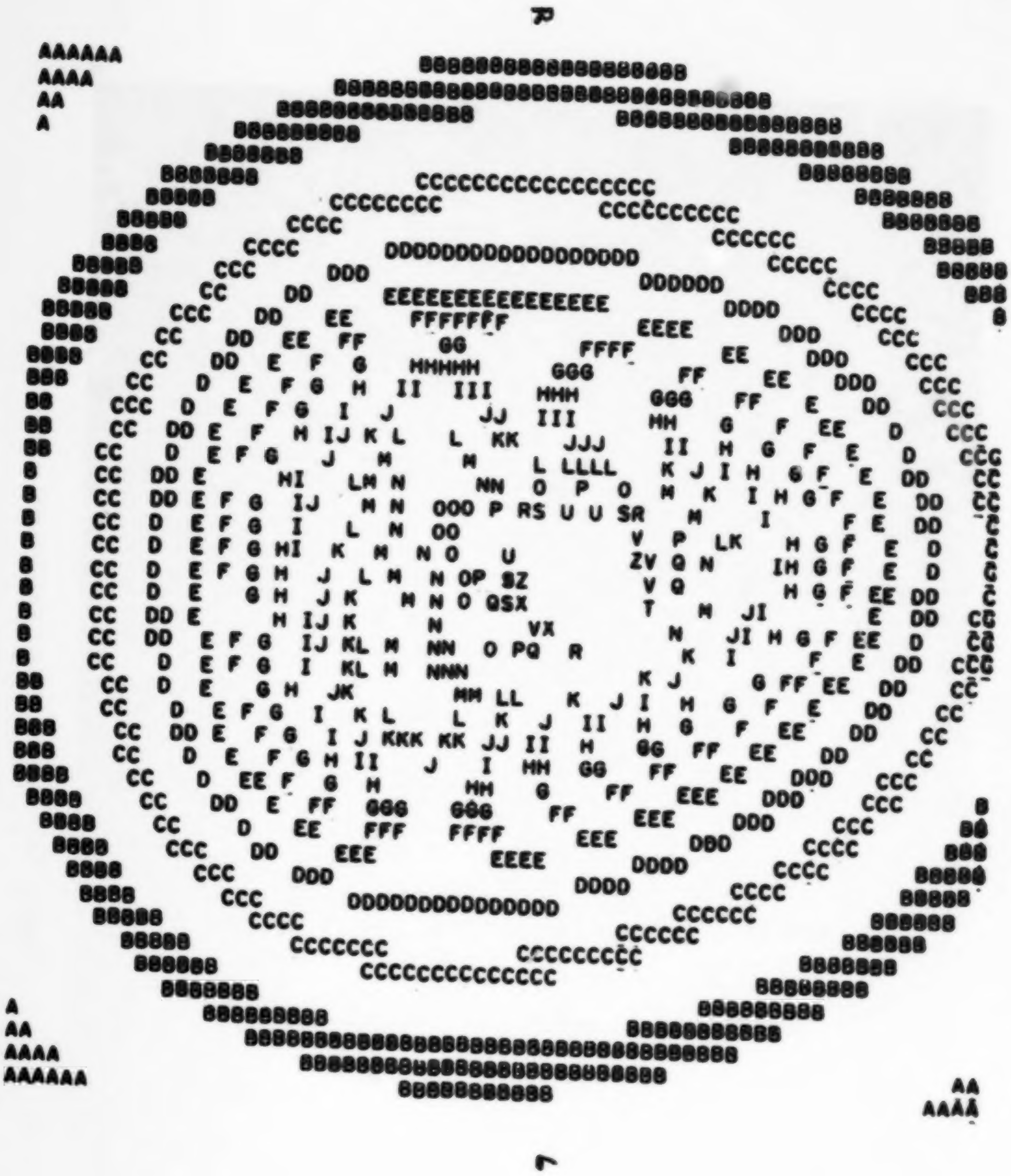

Figure 15. Computer printout - Sagittal plane, pelvis of patient (figure 13).

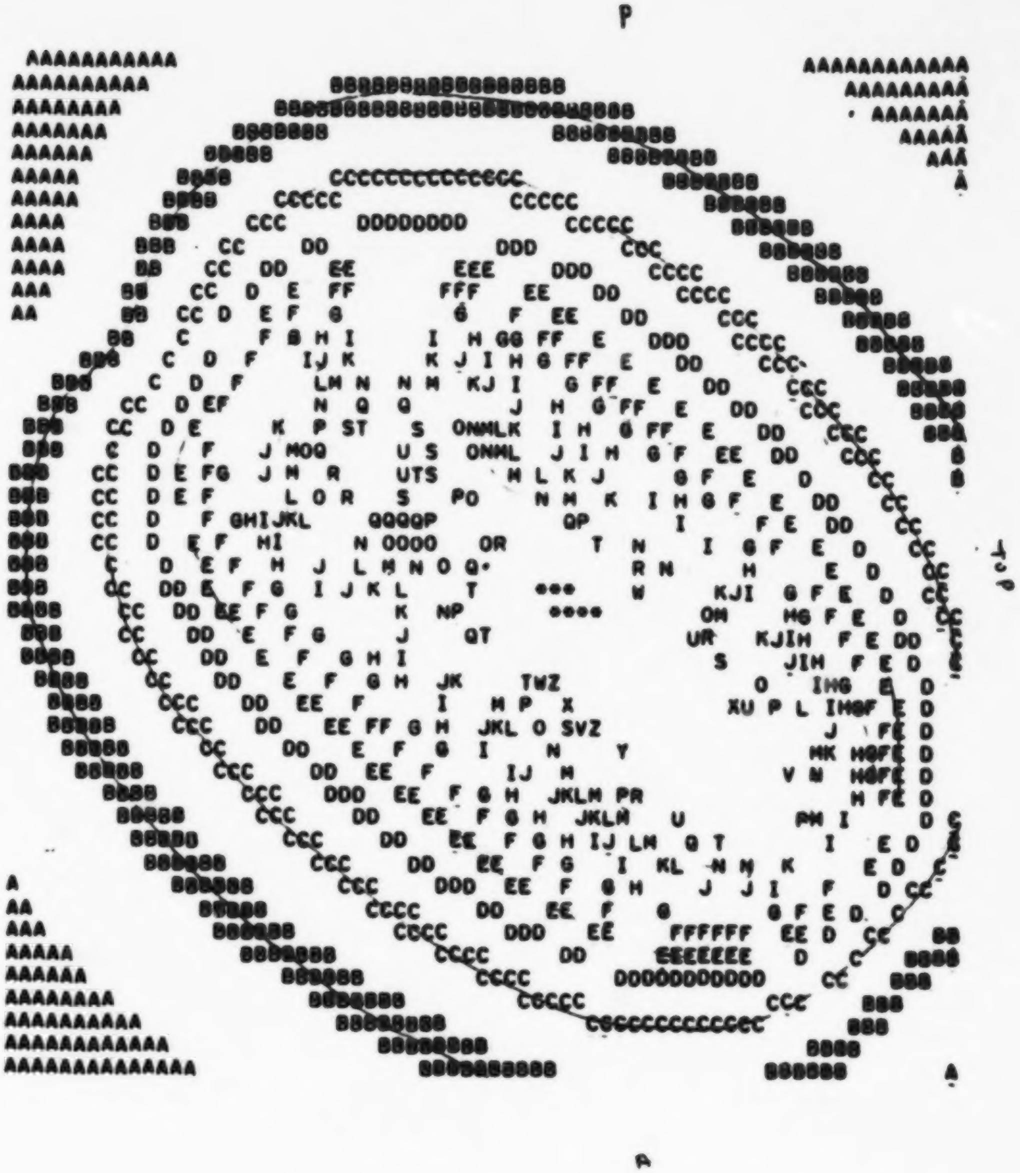

Figure 16. Computer printout - Coronal plane, pelvis of patient (figure 14).

CANCER OF THE UTERINE CORPUS

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INDICATION FOR RADIATION THERAPY IN THE TREATMENT OF CANCER OF THE ENDOMETRIUM

S. B. Gusberg, M.D., D.Sc.

The role of radiotherapy in the treatment of endometrial cancer is ill-defined and controversial. Efforts to clarify it must be aimed at establishing criteria for modalities offering the greatest rate of cure with the smallest risk of injury. It would appear, then, that we should devise a protocol of individualization that will not penalize the patient with a tumor of low virulence by overtreatment, nor one with a very aggressive lesion by undertreatment for fear of sequelae.

Some of our problems of reference in this area have related to staging inconsistencies, with attendant problems of selection in reporting and assessment.

In order to individualize therapy and compare results with those obtained in other treatment centers, a system of classification is essential. In addition to providing a means of standardized tumor description that permits communication among therapists, and prognosis, it must provide a clinically useful scheme that aids in selection of the best therapeutic regimen. Such a classification must consider and utilize the biologic properties of the tumor being studied, if the therapy chosen is to be adequate in combating the virulence of the tumor.

Three reliable factors in assaying virulence in corpus cancer are: (1) uterine enlargement, (2) lack of histologic differentiation of tumor, and (3) cervix involvement. Each of these factors can be shown to have a direct relationship to patient survival, and each is easily ascertained at the time of diagnostic curettage. Distribution of these factors acquires meaning when we see that 67 percent of the patients in our study group had an enlarged uterus, 18.3 percent had undifferentiated tumors, and 7.7 percent showed cervical involvement. In 29.7 percent there was deep invasion of the myometrium. There is linear correlation between lack of differentiation and depth of myometrial invasion, and the latter has been shown to correlate well with diminished survival.

It becomes readily apparent that the well-differentiated tumor with superficial penetration in the uterus of normal size is less virulent, and thus is more likely to respond to therapy, than the anaplastic tumor with deep myometrial penetration in the enlarged uterus. Although both tumors appear "confined to the uterus," on clinical examination, their response to therapy in terms of 5 year "cure rate" will be quite different. In order to individualize therapy by applying a more vigorous regimen to the more virulent tumors, we must have a classification that recognizes these important biologic parameters, and from which we can predict tumor behavior with more precision. Our treatment classification is shown in table 1.

In studying those tumors in each of the stages in terms of mode of spread, extent of spread at the time of surgery, response to therapy, and 5 year "cure rate," we have analyzed the biologic implication of such staging as follows:

Stage I: A localized, dependent tumor;
Stage II: Geographic spread = local extension;
Stage III: Biologic spread = lymphatic permeation;
Stage IV: Widespread, autonomous tumor.

With such a scheme in mind, it remains for us to find modalities of therapy that will properly treat the tumor variants.

RATIONALE OF COMBINED THERAPY

For almost a century hysterectomy has been the recognized treatment for endometrial cancer. Because of multiple medical deficiencies in the population at highest risk from corpus cancer, however, there always has been a significant number of patients with this disease who were considered unsuitable for surgery. The introduction of radium therapy provided an alternative, and experience in this modality accumulated in Stockholm during the 1930's. Swedish physicians referred to the Radiumhemmet not only patients whose medial disabilities contraindicated primary surgery, but those in whom the disease was far advanced. In 1941 Heyman reported his method of uterine packing, accompanied by a vaginal cylinder as a formal treatment mode. Kottmeier expanded this program into a definitive regimen. In a large study group reported in 1959, his center achieved an absolute cure rate of 63.3 percent with 68.2 percent living and well in the "operable" group, treated only by radiotherapy, except for recurrence in the uterus, where hysterectomy was employed.

While the Stockholm method did not include a planned combined treatment with surgery, it offered postoperative treatment to patients operated upon elsewhere and achieved a 5 year survival of 80.4 percent in this group. Furthermore, it provided therapy to patients with vaginal recurrence following hysterectomy, and in this group achieved a 5 year survival of 40.2 percent.

Stimulated by the Stockholm success, gynecologists in our country began to combine preoperative radiation therapy with total abdominal hysterectomy and bilateral salpingo-oophrectomy performed 4-6 weeks later. In the three decades that have passed since the inauguration of this trent, a large amount of data from the experience of combined therapy has accumulated. Unfortunately, much of this information loses its significance because of differences in classification schemes and treatment modes employed by the various therapy centers. This compels comparison of results within the single institution, thus fragmenting total experience in each mode and diminish its statistical significance.

Taking this into account, and remembering the spectrum of dissimilarity permitted within a single stage of some classification schemes, we have attempted to correlate the reports published from several clinics. The sum of this experience, even without analysis of the selectivity or quality of each sample, suggests an advantage of combined therapy over hysterectomy alone in the treatment of endometrial carcinoma. Our experience is presented in table 2.

In the analysis of published reports, one finds other parameters with which one can avoid the obstacle of varied classifications, and still gauge the radiotherapeutic contribution to combined therapy. These factors include the incidence of vaginal vault recurrence, and the "cure" rate in patients whose uteri have been rendered free of tumor as determined at the time of hysterectomy following radiotherapy.

In our own study group, there was a two-thirds diminution in vaginal vault recurrences in patients treated by combination therapy. This finding is supported by the experience at other centers (tables 3 and 4). Kottmeier reports recurrent tumor in 4 percent of 347 patients treated by hysterectomy, and then postoperatively by radium.

The capacity of preoperative radiotherapy to destroy corpus cancer has been well established by many investigators. Chau has found residual tumor in 28 percent of patients so treated. In our study group of 168 patients, 30 percent had no residual tumor at the time of hysterectomy, 57 percent had recognizable tumor showing radiation changes, and only 13 percent show no radiotherapeutic effect at all. Sandberg and McLennan report that after curettage alone 10 to 15 percent of uteri are found to be free of tumor at the time of hysterectomy. Noland, in 235 patients treated by hysterectomy alone following curettage, found only 4.6 percent free of tumor at the time of surgery. All this leaves little doubt about the capacity of preoperative radiation to "sterilize" the uterus.

Moreover, if we study "cure" rates, we find they are better when tumor has been destroyed prior to hysterectomy. In this context, Nolan reports an 89 percent cure rate in 97 patients with no residual cancer after combined therapy, and 75 percent cure rate in 32 patients with residual tumor. Our own study produced a 74.5 percent cure rate when cancer was absent after combined therapy, and a 50 percent cure rate when there was residual cancer at the time of hysterectomy.

With these data in mind, the advocates of combination therapy suggest the following advantages:

1. Devitalization of the surface bulk of tumor, reducing implantation spread and dissemination due to direct surgical manipulation;
2. Reduction in uterine size and increased retraction, facilitating surgical clearance of the specimen and preventing operative rupture;
3. Fibrosing of lymphatic and vascular channels, preventing operative spread;
4. Reduction in bleeding and prevention of tumor progression while patients with intercurrent medical dificiencies are rendered fit for surgery;
5. Apparent improvement in cure rate.

APPLICABILITY OF COMBINED TREATMENT

Our selection of treatment is based upon our tumor classification (table 1), for it appears to offer a systematic graded order of virulence. The marginal improvement in cure rate offered in Stage I has not persuaded us up to now that preoperative irradiation, a second anesthetic, and the 1 month interval we practice are in the patient's best interest. Whether postoperative vault ovoids in this stage would be beneficial is speculative.

In Stage II we have demonstrated clear improvement by a preoperative Stockholm (packing) plan.

In Stage III cancer of the endometrium we offer preoperative irradiation by radium packing, omitting vaginal ovoids to diminish the dose to the lower ureter. If the uterine cavity is larger than 10 cm, we omit radium but offer external irradiation by Betatron. Radiation therapy of either mode is followed in 4 weeks by radical hysterectomy and bilateral pelvic lymphadenectomy.

Since extension of Stage III tumors may take the route of parametrial channels to the deep pelvic nodes in a similar manner to cervix cancer, it seems reasonable to provide the patient with treatment appropriate to both corpus and cervix primaries. If excessive obesity, advanced age, or general disability reduces the patient's eligibility for radical surgery, we treat with radical radiotherapy as for cervix cancer and follow this with conventional hysterectomy. We have not encountered unusual technical difficulty or significant morbidity in this regimen.

It would appear that one can reconcile the apparent differences in reported treatment results, and define the role of radiotherapy in the treatment of endometrial cancer, by adoption of a pre-treatment classification scheme, based upon virulence indices of these tumors now available to any experienced gynecologic surgeon. Surely the molecular biologist and immunologist will soon provide us with more sophisticated parameters on which to base these important therapeutic judgments.

Table 1. Classification of endometrial cancer (Gusberg)

Stage	Description
I	Uterus normal size
II	Uterus mildly enlarged (cavity less than 10 cm)
III	Uterus markedly enlarged (cavity more than 10 cm)
IV	Contiguous organs involved or distant metastases

Note: Add one stage for anaplastic tumor or cervix involvement.

Table 2. General result in corpus cancer (Gusberg)

Treatment	Number of patients	Living and well at 5 years (percent)	Relative cure rate (percent)
Hysterectomy	191	56.5	64.2
Radium and hysterectomy	219	69.4	83.0

Table 3. Vaginal recurrences following therapy, two treatment modes in one center

Author	Treatment	Number of patients	Vaginal recurrences (percent
Gusberg	Hysterectomy	191	14.6
	Combined therapy	219	4.5
Boutselis	Hysterctomy	61	14.7
	Combined therapy	208	1.8
Wade	Hysterectomy	43	9.3
	Combined therapy	156	1.9

Table 4. Vaginal recurrences following therapy

Author	Treatment	Number of patients	Vaginal recurrences (percent)
Meigs	Surgery	206	12.1
Way	Surgery	102	17.7
Javert & Douglas	Surgery	381	10.4
Kottmeier	Combined therapy (post op)	347	4.0
Rutledge	Combined therapy	215	1.5
Chau	Combined therapy	95	2.1

RADIUM IN CARCINOMA OF THE UTERINE CORPUS

H. L. Kottmeier, M.D.

Choice of therapy in carcinoma of the endometrium is dependent on the general condition of the patient, the stage of the disease, the size of the uterine cavity, and the maturity and differentiation of the cancer. A curative treatment may be surgery, irradiation, or a combined treatment of surgery and radiation. As far as radiation is concerned, intracavitary application of radioactive sources in the uterine cavity and/or vagina can be applied, as well as external radiotherapy.

At the Radiumhemmet we consider primary panhysterectomy with salpingo-oophorectomy followed by postoperative irradiation as a treatment of choice in cases of carcinoma of the corpus, limited to the corpus in Grades I and II. Experience has revealed that in such cases the carcinoma as a rule is superficially growing into the myometrium, and metastases are not seen in regional pelvic lymph nodes. Recurrence may, however, occur in the vagina months or years after surgery. We have observed such recurrences in only 2 of 105 patients who received postoperative irradiation, in contrast to 6 out of 39 cases where no irradiation was given.

In our experience, the simplest way to apply irradiation is in the postoperative period. A cylinder containing radium is inserted into the vagina about 10 days following surgery. This procedure can be carried out without anesthesia. Radiation is given to the whole vagina, since recurrences are seen most frequently in the vault and in the tissues surrounding the urethra. The length and the diameter of the stainless steel cylinder depends on the size of the vagina. Our applicators contain 100 to 200 mg of radium. The filter is 2 mm of lead. About 2,300 rads are given in a depth of 1.5 cm from the outer surface of the vaginal cylinder (figures 1 and 2).

In the years 1962 to 1963, a total of 198 patients were treated with primary panhysterectomy and intravaginal radium given postoperatively (table 1). In 174 of these 198 cases, the gynecologist believed that the cancer was limited to the corpus. Histological examination revealed a more or less differentiated adenocarcinoma, Grade I and II, in these cases. After 5 years, 153 of the 174 patients (87.9 percent) were alive and without evidence of the disease.

Carcinoma of the corpus may extend to the vagina. Metastases or recurrences are seen most frequently in the vault of the vagina, in its anterior wall, and in the tissues surrounding the urethra. Investigation has revealed that such metastases or recurrences are due to lymphatic spread of the cancer and not, as a rule, to spills of cancer cells. This should be taken into consideration when treating recurrences to the vagina. It is important to treat the full length of the vagina, where implantation of radioactive needles is not proper therapy. A combination of local application of radium and external, carefully planned irradiation may lead to satisfactory results. We give a dose of 3,000-3,500 gamma R to a depth of 2 cm in 20-30 hours, and administer in addition a dose of 3,500-4,000 rad of external radiation over a period of 4 weeks. A 5-year corrected survival rate of 40.3 percent has been achieved in 153 cases of vaginal recurrences.

Many gynecologists recommend preoperative irradiation with radium in all cases of carcinoma of the endometrium. It has been our policy to limit postoperative irradiation in cases of carcinoma of the corpus to Grades 1 and 2. This type of treatment is simple and cheap, the results are good.

Radiation, on the other hand, should be the primary treatment of choice in all cases of carcinoma of the endometrium in which the growth had extended to the isthmus and endocervix, or to other tissues in the pelvis. This is also valid in cases of anaplastic and immature carcinoma. It is the treatment of choice in all patients with systemic disease. Careful planning must precede any kind of irradiation. Such planning includes clinical examination under anesthesia, hysteroscopy, fractional curettage, needle aspiration biopsy from findings outside the uterus, and x-ray examinations. In Stages III and IV, external irradiation may be the primary treatment, perhaps combined with injections of progesterone.

In the great majority of cases of carcinoma of the endometrium, the primary radiation treatment is the insertion of radioactive sources into the uterine cavity and vagina. It is not easy to apply radium properly to an endometrial carcinoma and deliver a cancericidel dose to cancer in the uterine wall. The uterine cavity is often enlarged and irregular, and a tandem will be ineffective in an enlarged uterine cavity (figure 3).

It is important to remember that anaplastic carcinoma of the endometrium tends to invade the myometrium deeply at an early stage. Many different techniques have been tried. At Radiumhemmet for years we used a single irradiation into the uterine cavity, with unsatisfactory results. In 1941, Heyman and Benner introduced the intracavitary method. The principle was packing the uterine cavity with multiple irradiators. They designed four different sizes of irradiators with a diameter of 7.8 - 13.8 mm. In 1941 and subsequent years Heyman demonstrated that the results had remarkably improved.

Basically we maintain this technique, but in recent years it was further developed. Experience has shown that satisfactory results are achieved in all cases where an enlarged irregular uterine cavity is packed with tubes of more than 7.8 mm in diameter. It has been shown that it is necessary not only to fill the cavity entirely, but even to distend the walls of the uterus. This can easily be done, especially in cases there the carcinoma has deeply invaded the myometrium.

A stainless string is connected to each irradiator. These strings are held by the operator in the left hand. After introducing and packing the uterine cavity with a number of irradiators, a Hegar 2 dilator is introduced between the capsules in the uterine cavity. Careful dilatation permits the insertion of several more capsules, provided the cancer has deeply invaded the myometrium. Consequently, it is possible to distend the uterine cavity and decrease the distance from the radium to the cancer. Radiographic examinations of the uterus with simultaneous pneumoperitoneum have shown that it is possible to reduce the wall thickness to one-third of normal value. The risk of perforation can be tolerated providing the dilatation is carefully carried out and no force is used. Perforation sometimes occurs at the time of curettage, and occasionally makes satisfactory packing difficult. Perforation at the time of uterine packing is rare.

With this technique, a great number of the capsules can be located close to the endometrium with a rather good dose rate gradient across the myometrium in all planes, including that perpendicular to the capsule, that forming an oblique angle with the capsule, or one through the axis of a capsule. The dose at the distance of 1 cm from the endometrium is about 53 percent, depending upon the irradiator in direct connection with the uterine wall involved.

The handling of the radium irradiators brings some protection problems for both the operator and assisting nurses. Hence in recent years radium has been replaced by cesium 137. These irradiators have a length of 30.5 mm and a diameter of 7.8 and 9.8 mm, respectively (figure 4). The small capsule, loaded with 35 mCi of cesium, is intended for packing the uterine corpus cavity. The larger irradiator, loaded with 85 mCi of cesium, is used for the endocervix. Removal of the irradiators is easier, providing the endocervical irradiator has a diameter larger than that of the corpus cavity. The wall of the irradiator is stainless steel in order to decrease secondary beta radiation. The filter is equivalent to 2 mm of lead. The irradiators are placed in a mobile radium safe. A lead screen protects the operator and assisting nurse during the course of packing. Measurements have revealed only small doses of irradiation to the doctor and nurse. The largest dose was 111 milliroentgens (in the case of a patient packed with 7 cesium irradiators) registered on the top of the left index finger. The dose on other parts of the body was much less.

The principle of the packing method is to deliver a comparatively high dose to the cancer in the uterine wall without damage to surrounding normal tissue. The determinations were made in phantoms in air in the vicinity of leather bags filled with a few or multiple applicators. In addition, direct measurements of the dose rate were carried out on 19 patients in whom a laparotomy was performed with irradiators in place, using the Siemens gammameter probe with a small cadmium surface crystal. The object was to determine the relative values of the average intensities for a number of different combinations of irradiators and treatment time giving equal doses in different cases.

The radium dose that we wish to apply amounts to about 1,300 rads at a distance of 1.5 cm from the surface of the nearest irradiator to the endometrium. The packing is repeated two or three times, 3 weeks apart. Three applications are carried out in patients considered clinically inoperable because of age or extra-genital complications. In cases of carcinoma of the corpus extending to surrounding tissues, the main treatment consists of external irradiation and only one packing (figure 5).

In addition to the packing of the uterine cavity, radium is inserted into the vagina. This type of the intracavitary irradiation does not differ from the treatment applied to patients in whom a primary panhysterectomy had been carried out.

An enlarged uterine cavity is found especially in cases of poorly differentiated endometrial carcinoma, but it also occurs in other cases. Gusberg et al have proved that there is a correlation between the length and size of the uterine cavity, and the prognosis. I have mentioned that Heyman increased the diameter of the irradiators in order to facilitate packing a large and irregular cavity. A study of cases treated with such irradiators at the Radiumhemmet demonstrated that a satisfactory result was attained only in exceptional cases. I believe that the explanation for the poor results is the fact that large capsules do not permit satisfactory packing and stretching of the uterine cavity. The dose distribution in the uterine wall consequently will be unsatisfactory, compared with cases in which the uterine wall has been distended. The purpose of the initial treatment must be to shrink the uterine cavity.

This can be carried out by two methods. One is to shrink it by planned external irradiation. In recent years we have attempted this technique, but the results have not been convincing. Another method initiated several years ago is to insert a tandem with radioactive sources into the uterine cavity. The patient is asked to turn in bed so the irradiator may move from one place to another. Radium dosages from 3,000 to 3,500 mg-hours are delivered by this intrauterine tandem. Three weeks later the patient is reexamined. As a rule the cavity is much smaller, so the first packing of the standard cesium capsule is performed. The packing is done exactly as described, with total disregard for the amount of radiation from the initial intrauterine tandem. The packing is repeated two or three times.

Intracavitary application of radium with a tandem or cylinder has been administered with the remote afterloading machine of Walstam in a small number of cases, but afterloading is not used at present.

In addition to intracavitary application of radioactive sources, external irradiation is given in cases where the cancer has extended to the endocervix, to the vagina, or to other tissue. Surgery may follow irradiation therapy, especially in instances of anaplastic tumors limited to the corpus. As a rule, panhysterectomy and bilateral salpingo-oophorectomy are carried out about 6 weeks after completion of intracavitary radiation.

In the years 1962-1963 some 360 cases of primary carcinoma of the endometrium were treated with irradiation at the Radiumhemmet (table 3). There were 213 Stage I cases, 78 in Stage II, 45 in Stage III, and 24 in Stage IV. About 110 of the 360 patients were considered poor operative risks because of old age, marked obesity or severe extra-genital disease. A total of 211 of these patients (58.6 percent) are still alive after 5 years without evidence of the disease. Thirty-six patients died from intercurrent disease. The 5-year cure rate figure for Stage I is 71.8 percent; for Stage II, 56.4 percent; for Stage III, 24.4 percent; and for Stage IV, 12.5 percent. Histological examination revealed a Grade I adenocarcinoma in 34 cases, of whom 31 are symptom free at 5 years, and 3 have died from disease. In 181 cases the carcinoma was classified as Grade II. A total of 122 of the 191 patients (64 percent) survived 5 years.

It should be noted that 65 of the 191 patients of this grade were considered poor operative risks. Twenty of them died from intercurrent diseases. In as many as 135 cases the carcinoma was immature, anaplastic, or sarcoma-similar. In 39 of these 135 cases the cancer had extended to other organs and was completely inoperable. At the end of 5 years 58 of the 135 cases are symptom-free, a cure rate of about 43 percent.

Panhysterectomy, including removal of the adnexa, has been performed 5 weeks to several months after completion of radiation. It was performed in 156 of the 360 cases. There were 114 Stage I cases, 21 Stage II, 19 Stage III, and 2 in Stage IV. In 76 of the Stage I cases, 14 Stage II, and 5 Stage III cases histological examination did not show any remnants of the growth. In 11 of the remaining cases examination revealed residual cancer localized to extra-pelvic tissues. The great majority of residual cancer cases showed marked degenerative changes (table 4).

Complications may appear as a sequel to both surgery and radiotherapy. A vesico-vaginal fistula has occurred in 8 patients, of whom 6 had been treated by radiation and surgery. Nine patients have had a recto-vaginal fistula; in 7 of these patients combined surgical and radiation approach has been carried out.

I have emphasized that cases with a much enlarged uterine cavity have a poor prognosis. Methods have been described for shrinking the uterine cavity prior to the application of definitive therapy. In the cases in this series the method of choice has been intrauterine application of a radium tandem. Experience has shown that application of more than 15 cesium tubes will not render satisfactory results. In 38 Stage I cases a tandem was applied in order to shrink the cavity. Twenty-three of these 38 cases were symptom-free after 5 years. The corresponding figures for Stage II are 30 and 16 patients; for Stage III, 19 and 3; and for Stage IV, 15 and 3. In 57 of the 102 cases with an enlarged cavity, the cancer was anaplastic in nature.

Two other complications that may influence treatment should be mentioned. Perforation of the uterine cavity has been reported in 36 of the 360 cases. In 5 of these cases the perforation was due to the cancer. In 26 others the perforation occurred during exploration of the uterine cavity, as a rule prior to admission to the Radiumhemmet. No complications have been registered, though a slight increase in temperature was observed in 8 instances. Finally, in 4 cases a perforation occurred in connection with packing of the uterine cavity. In 3 of these 4 cases there were no complications. In the last case an unusual incident occurred. The string to one of the irradiators broke, and the irradiator penetrated the peritoneal cavity through the perforation. A laparotomy was performed, the irradiator was extracted from the abdomen, and treatment proceeded in the usual way. The patient is still living without any evidence of the disease.

Pyometra sometimes is found in cases of endometrial carcinoma. Marked pyometra was diagnosed in 21 of the 360 cases. In 2 of those, the pyometra was complicated by septic fever. The uterine cavity was drained to the vagina, and radium introduced 1 or 2 days later. Nine of the 21 patients are still alive without evidence of the disease for 5 or more years.

SUMMARY

A survey is made of Radiumhemmet experience with intracavitary radiation in the treatment of carcinoma of the endometrium. Emphasis is placed on the individualization of therapy. Attention should be paid to the general condition of the patient, the extent of the cancer, the size and length of the uterine cavity, and the maturation and differentiation of the growth. A total of 559 cases of carcinoma of the endometrium were seen at the Radiumhemmet in the years 1962-1963. Some 381 of these patients are symptom-free after 5 years, a cure rate of 68.2 percent. Some 46 patients (8.2 percent) have died from intercurrent disease. The corresponding Stage I figures are 392 and 310, a 5-year cure rate of 79.1 percent. About 9.9 percent of the 392 patients have died from intercurrent disease (table 5).

Table 1. Carcinoma of the endometrium 1962 - 1963
(Primary Surgery + Irradiation)

Invasion of the Cancer into the Uterine Wall	HISTOLOGIC GRADING							
	I		II		III		TOTAL	
	No. of Cases	Living at 5 yrs	No. of Cases	Living at 5 yrs	No. of Cases	Living at 5 yrs	No. of Cases	Living at 5 yrs
Superficial	56 (90.3%)	54	43 (38.4%)	40	2 (8.3%)	2	101	96 = 95.6%
Moderate	4 (6.5%)	4	53 (47.3%)	43	12 (50.0%)	9	69	56 = 81.2%
Deep	2 (3.2%)	2	16 (14.3%)	10	10 (41.7%)	5	28	17= 60.7%
Total n:r of Cases	62	60=96.8%	112	93=83%	24	16=66.7%		

Table 2. Dose to personnel handling newer cesium 137 source

	Operator mrad	Assistant nurse mrad	Assistant operator mrad	Assistant at removal mrad
Top left index finger	110	45	55	100
Top fourth finger	-	-	-	55
Left thumb	95	20	-	-
Left hand outside	85	15	-	-
Left hand inside	55	15	-	-
Top right index finger	60	30	65	75
Top fourth finger	-	-	-	45
Right thumb	55	45	-	60
Right hand outside	70	30	-	-
Right hand inside	50	20	-	40
Gonad	-	10	-	10

Table 3. Carcinoma of the endometrium cases primarily treated at Radiumhemmet 1962-1963

Histologic grading		Clinical stage																			
		I				II				III				IV				Total			
		No. of cases	5 year survival No.	%	Interc. death	No. of cases	5 year survival No.	%	Interc. death	No. of cases	5 year survival No.	%	Interc. death	No. of cases	5 year survival No.	%	Interc. death	No. of cases	5 year survival No.	%	Interc. death
Grade 1	Oper.	25	24		1	1	1											34	31		3
	Clin. inop.	8	6		2																
	Inop.																				
Grade 2	Oper.	72	63		3	30	17		1	4	3			1	1			191	122		20
	Clin. inop.	48	25		14	17	9		4												
	Inop.									12	3			7	1						
Grade 3 + 4	Oper.	35	25		4	19	12			5	2							135	58		13
	Clin. inop.	25	10		6	11	5		1	1											
	Inop.									23	3		2	16	1						
Total cases	Oper.	132	112	84,8	8	50	30	60,0	1	9	5	55,6		1	1						
	Clin. inop.	81	41	50,6	22	28	14	50,0	5	1											
	Inop.									35	6	17,1	2	23	2	8,9					
Total		213	153	71,8	30 14,1	78	44	56,4	6	45	11	24,4	2	24	3	12,5		360	211	58,6	10,9%

Table 4. Carcinoma of the endometrium 1962-1963
(Radiation + Surgery or only Radiation)

Clinical stage

Histologic grading		I			II			III			IV		
		No. patient	5 year survival No.	%	No. patient	5 year survival No.	%	No. patient	5 year survival No.	%	No. patient	5 year survival No.	%
Grade 1	Oper. no resid. ca.	21	20	95	1	1	100						
	Oper. resid. or recurr. ca.	1	1	100									
	No oper.	10	8	80									
Grade 2	Oper. no resid. ca.	38	37	97	5	4	80	1	1	100			
	Oper. resid. or recurr. ca.	24	17	71	5	2	40	7	3	43	1	1	100
	No oper.	58	35	60	37	20	54	8	2	25	7	1	14
Grade 3 + 4	Oper. no resid. ca.	17	15	88	8	6	75	4	2	50			
	Oper. resid. or recurr. ca.	13	7	54	2	1	50	7	2	28	1	1	100
	No oper.	31	14	45	20	10	50	18	1	5	15	0	0
Total cases	Oper. no resid. ca.	76	72	95	14	11	79	5	3	60			
	Oper. resid. or recurr. ca.	38	25	66	7	3	43	14	5	36	2	2	100
	No uper.	99	57	57	57	30	53	26	3	12	22	1	5

Table 5. Carcinoma of the endometrium. All cases examined and treated at the Radiumhemmet in 1962 and 1963

	Stages I	II	III	IV	Total
Number of Cases	392	87	58	22	559
Symptomfree at 5 years	310 79.1%	52 59.8%	16 27.6%	3 13.6%	381 68.2%
Dead from Cancer	43 11.0%	30 34.5%	40 68.9%	19 86.4%	132 23.6%
Dead from Intercurrent disease	39 9.9%	5 5.8%	2 3.5%	-	46 8.2%

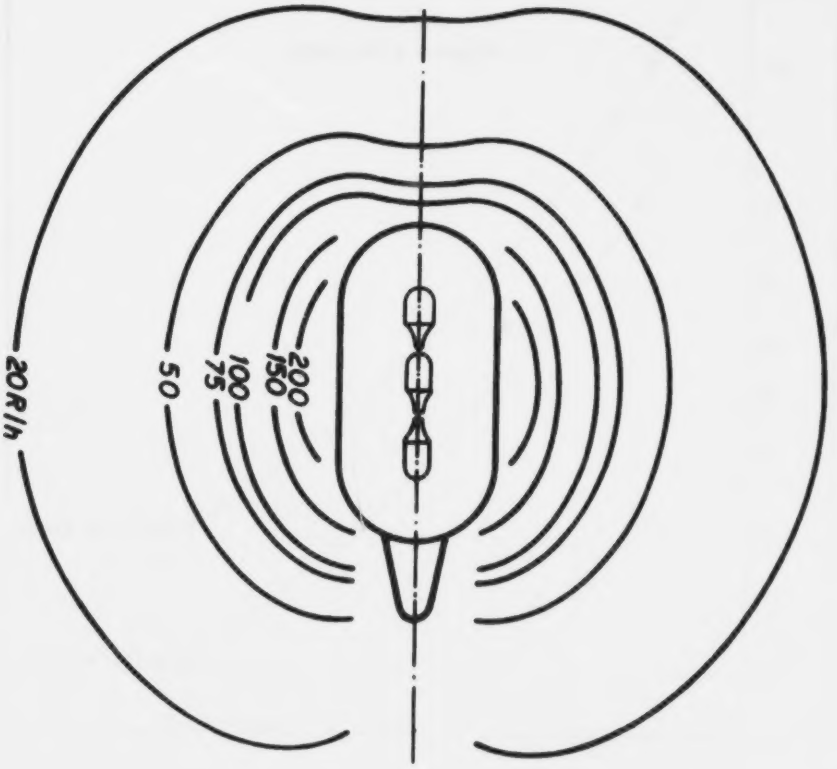

20R/h
50
75
100
150
200

Figure 1. Isodose around vaginal applicator

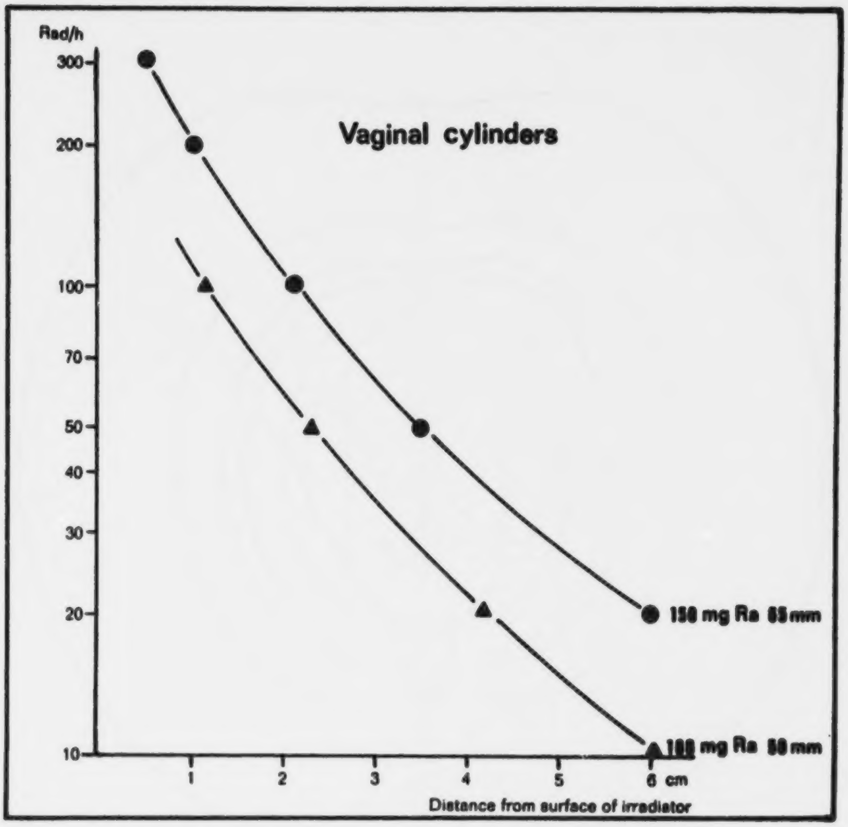


Figure 2. Dose distribution around vaginal applicator

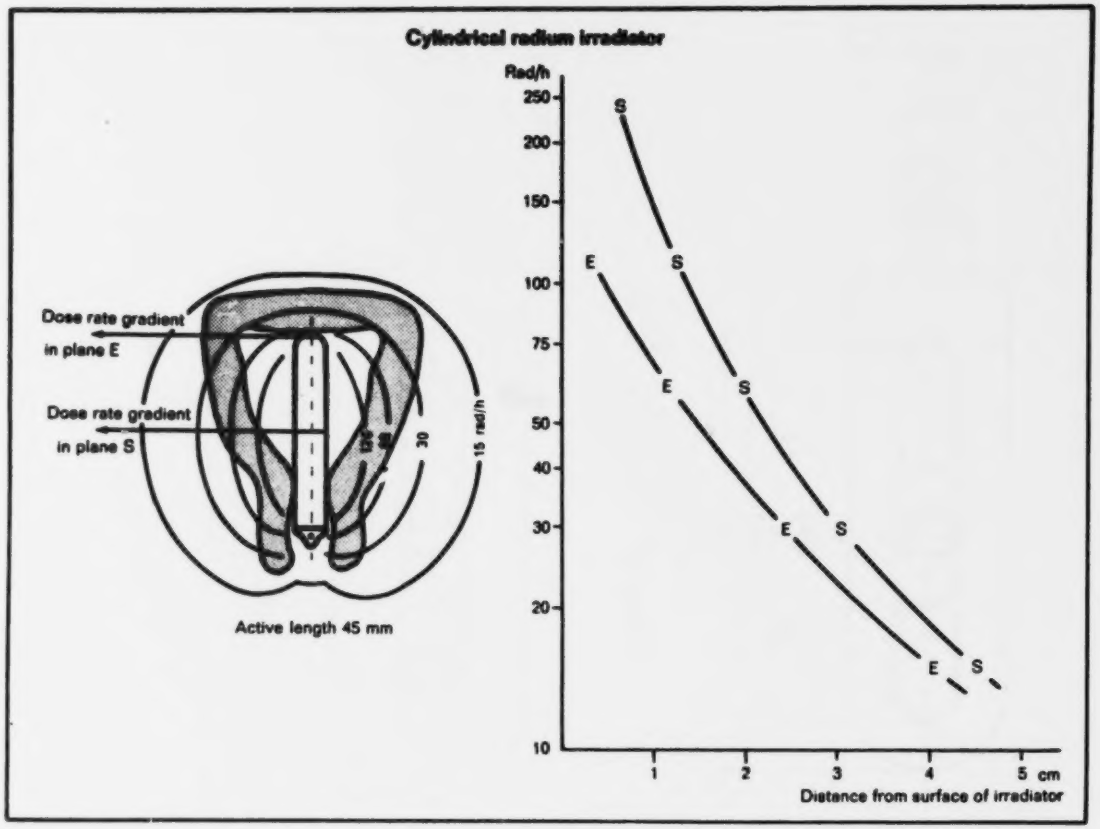
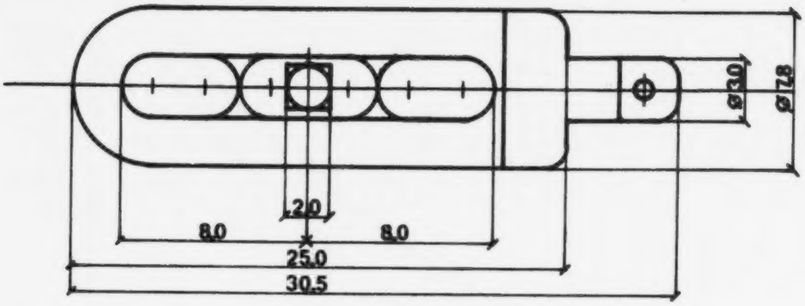


Figure 3. Dose distribution around an intrauterine tandem

Filter 1 35mCi ^{137}Cs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Ø7.8
2.0
8.0
8.0
25.0
30.5

Filter 2 84mCi ^{137}Cs

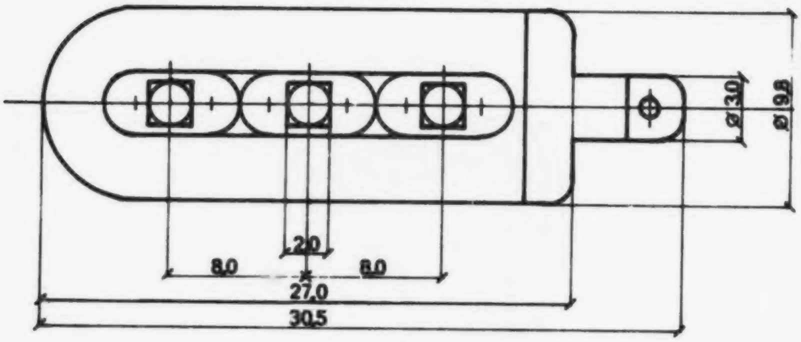
Ø3.0
Ø9.8
2.0
8.0
8.0
27.0
30.5

Figure 4. Cesium 137 replacements for radium

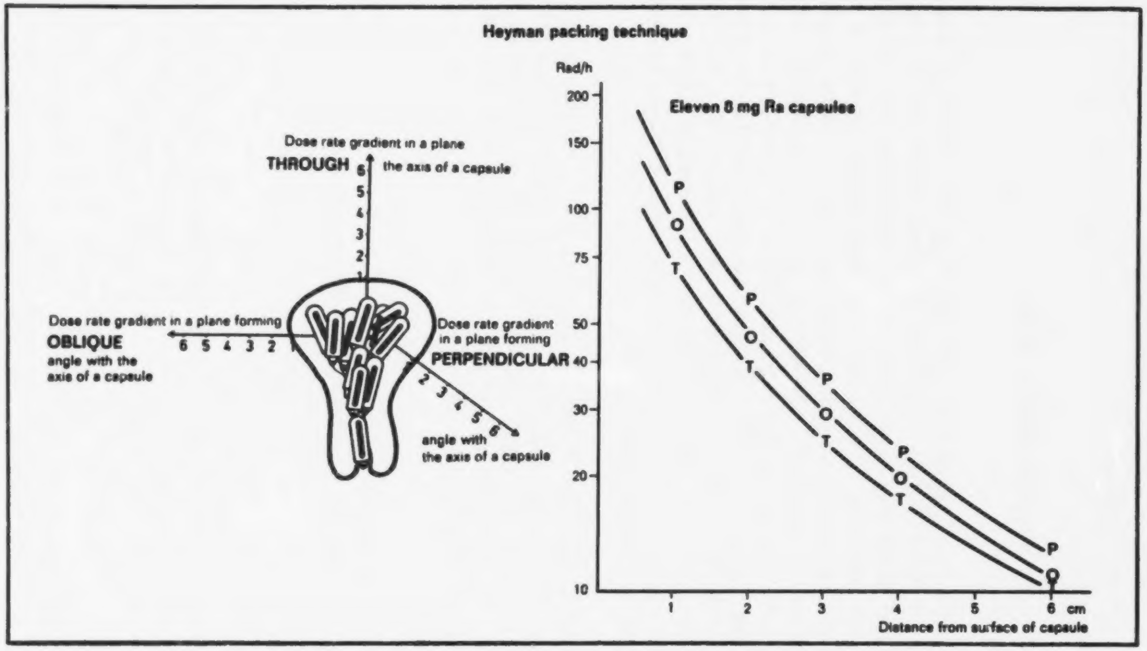

Figure 5. Heyman packing technique

AFTERLOADING THE UTERINE CAVITY
WITH MULTIPLE IRRADIATORS

Norman Simon, M.D.

Although the classic procedure of packing the uterine cavity with Heyman capsules containing radium has been used for decades, radiotherapists have some reservations. The capsules are highly radioactive; the unnecessary and excessive radiation exposure to operating room personnel has been acceptable only because packing the cavity with capsules is more effective than an ordinary tandem. Virtuoso surgeons and radiotherapists are able to keep radiation exposure to themselves and their associates at low levels by inserting the radium capsules with gun-fire rapidity and accuracy, but it takes many years of practice (and exposure) to develop this efficiency. It is a difficult technique to teach, while both teacher and student are exposed to radiation.

The Heyman applicator is a metal capsule 6 to 10 mm in diameter, containing radium. When the capsule is packed into the uterine cavity, a steel wire extends through the cervical os and vagina, and out the introitus. As many as 15 of these capsules may be inserted into the cavity; upon completion of treatment, they are removed by pulling on the wires.

Radium sources are dimensionally too large for afterloading multiple capsules in the uterus. The specific activity of radium is too low, the capsules needed to contain it and its gaseous daughter must be too large. Except in large-bore tandems, radium is unsuitable for afterloading the uterine cavity.

Our modification of the Heyman capsule allows afterloading the uterine cavity. The afterloading device is a plastic tube with a bulbous end dimensionally the same as a classical Heyman capsule (6 mm in diameter). The outer diameter of the plastic tube is 1.65 mm, and it contains a dummy obturator of steel tubing (18 gauge hypodermic needle stock) 1 mm in diameter. When the bulbous-ended tubes are packed into the cavity, the obturators are removed and a similar steel tube containing radioactive material is inserted into each tube and capsule.

The radioactive material we use is cesium 137 in Vycor glass, and miniaturization of the sources is of primary importance. Vycor glass is porous and sponge-like. The cesium is incorporated into a glass cylinder 0.7 mm in diameter; a 1.5 cm length of source is equivalent to 10 mgm of radium (25 mCi of cesium 137). The glass rod is annealed so there is no radioactivity on its surface, then encapsulated within the end of the 18-gauge steel tubing.

Although we prefer cesium, cobalt can be similarly used. It can be made cheaply and dimensionally small enough to fit in our afterloading capsules. But cobalt 60 has a half-life of only 5 years, and thus too short a shelf-life; energy is greater than that of cesium 137, thicker shielding is required. In contrast, cesium 137 has a half-life of 30 years, and replenishment should be required no oftener than for radium, where leakage makes re-encapsulation prudent at intervals as frequent as every 5 to 10 years.

Under ordinary circumstances, a patient suspected of cancer of the endometrium is admitted to the hospital complaining of vaginal bleeding. A dilatation and curettage is done under general anesthesia. If a diagnosis of cancer is established, and intracavitary radiation indicated, the patient is re-anesthetized and Heyman radium capsules are packed into the uterine cavity.

With afterloading devices, the empty capsules are inserted into the patient during her D and C. When the pathology report confirms the diagnosis of carcinoma, the radioactive sources are inserted. Thus the patient is spared a second operation. Aside from other advantages of afterloading, saving the patient another general anesthesia may be significant or crucial, for many patients with cancer of the endometrium are poor operative risks. Irradiation of the vault or even the whole vagina can be accomplished in this fashion.

All generally used colpostats can be adapted for our afterloading system, the 1.65 mm diameter plastic tubing inserts into any of the vaginal applicators. We have used our system in Manchester ovoids, the French rubber colpostat, Silverstone colpostat, and Ernst applicator.

Dose systems in the treatment of cancer of the endometrium stem from the guidelines of Heyman. The amount of irradiation from the intracavitary capsules is specified in mgm hrs, dependent upon the size of the uterus and number of capsules packed in it. Our technology in dosimetry has reached the stage where we can readily map out isodose surfaces and contours around sources in the uterus. The computer has provided us with rapid read-outs of the distribution of radiation.

Unfortunately, we are not able to specify the anatomy and pathology clearly enough to take full advantage of the data. The shape and thickness of the uterus and geometry of the tumor is rarely known with sufficient accuracy to use all our information in adjusting the time of exposure to intracavitary radium. In practice, calculations of dose are based on the selection of arbitrary distances from the multiple sources, and this method has yielded no reported improvement in results over the years. Even the position of important and vulnerable adjacent organs like bladder and gut are not well enough defined to enable us to improve on the empirical guidance of Heyman. Investigations by Joelson of the Radiumhemmet, and Collins of Texas, are leading us into newer pictures of the relationship of bladder and rectum to radium system.

Dosimetry in the vagina is another matter. The vaginal applicators are geometrically regular, and an absorbed dose in rads at the vaginal or applicator surface can be specified.

Which patients are suitable for the packing technique? Gusberg has pointed out that minimal lesions, well differentiated and localized in a small uterus (Stage I), may have as good results with hysterectomy alone as with a combined technic; but that the most commonly encountered tumors (Stage II) with larger uteruses up to 10 cm in length of cavity, or even smaller with less differentiated tumors, should benefit from the Stockholm technique. Other observers suggest that preoperative external radiation, particularly with megavoltage equipment, yields results as good as those of uterine packing. Gusberg crystallizes the problem in the treatment of cancer of the endometrium when he states: "The question most debated is whether preoperative intracavitary radium improves the results obtained by operation alone."

The disenchantment of many radiotherapists regarding packing of the uterine cavity with radium capsules has been due to the personnel dose (20-100 mrads) received in handling as much as 100 mgms of radium during the packing procedure. Elimination of radiation exposure to personnel promises to make preoperative packing of the uterine cavity a more widely used procedure.

Another advantage of afterloading is its adaptability for clinical investigation of the preferable time after radiation for hysterectomy. Traditional intervals of 4 to 6 weeks may have little more to offer than custom. Perhaps immediate operation after radiation, a more economical and less emotionally disturbing time relation for the patient, is equally good. Whether the tumor can be identified at operation has been used as an index of the efficacy of preoperative radiation. But this guideline, never too satisfactory, no longer would be useful if patients were operated on immediately after radiation.

Afterloading of the uterine cavity makes it more feasible to study randomized series of patients with endometrial carcinoma treated with and without loading the cavity with radioactive material, a study sorely needed to definitively establish the benefits of intracavitary radiation.

In summary, afterloading Heyman-type capsules have been developed, along with miniaturization of radioactive sources, to replace radium. Exposure of personnel to radiation while packing the uterus now is unnecessary. Accuracy of packing the uterine cavity is improved when the radiotherapist or surgeon is undistracted by radioactively "hot" material. The safety aspects of afterloading should provide opportunity for deliberate clinical research into problems of indication for intracavitary radiation, and time and dose relationships.

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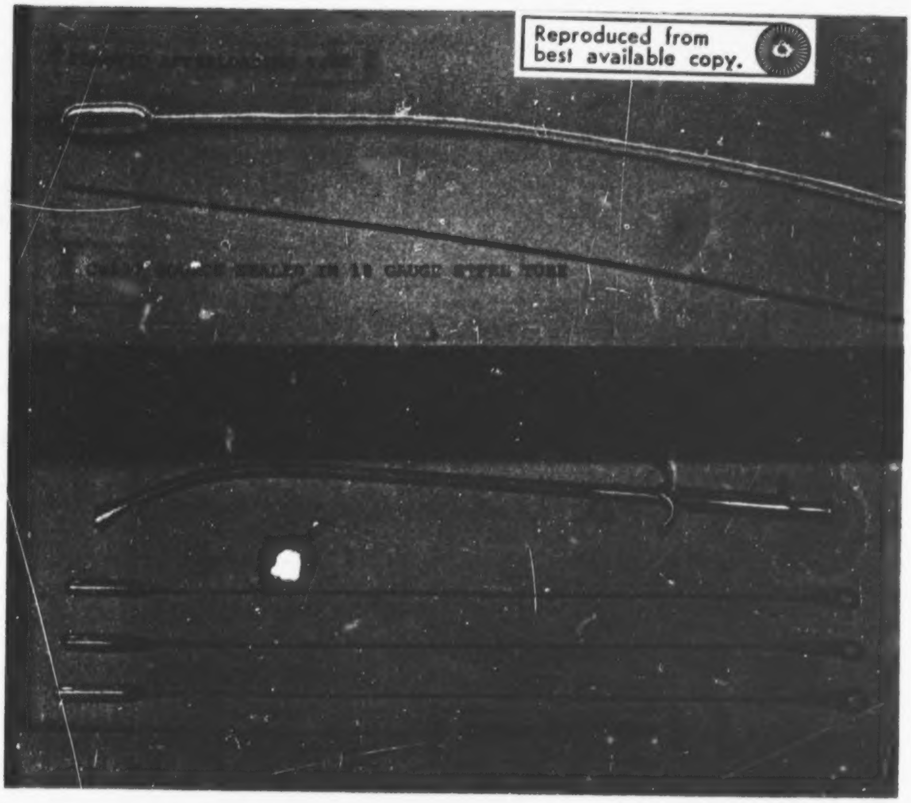
[illegible] SOURCE SEALED IN 18 GAUGE STEEL TUBE

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Figure 1. Modified plastic afterloading intrauterine applicator above with the commercially available Heyman applicator below. The introducer above the Heyman applicators is not needed when the plastic afterloaders are used.

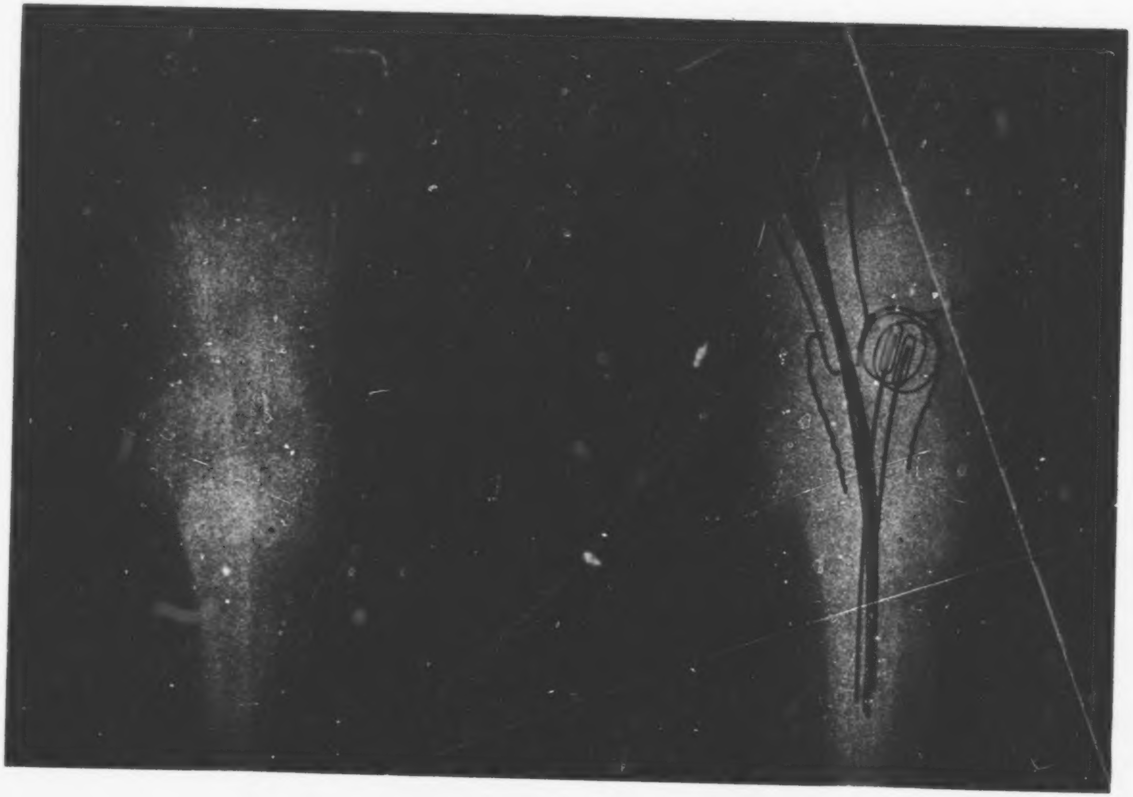

Figure 2. Lateral view of afterloading multiple irradiators in fundus of uterus. Each of the 7 intrauterine capsules (IC) contains 10 mgm Ra equivalent (25 mCi cesium 137). The Manchester ovoids (MO) also contain 10 mgms Ra equivalent in each.

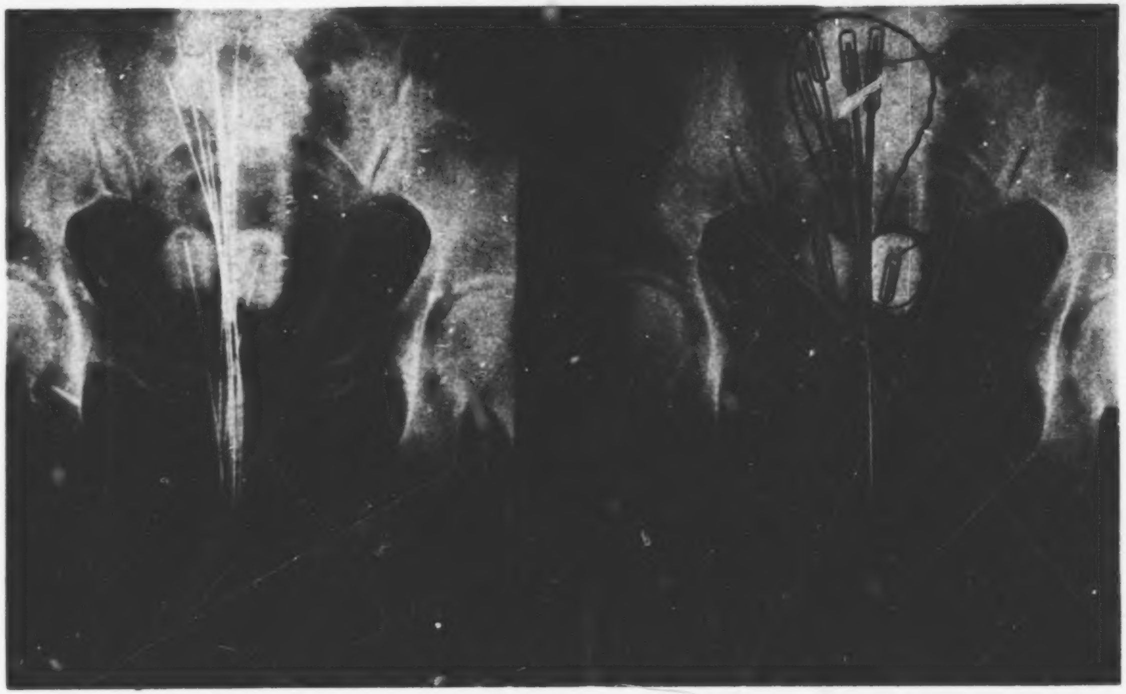

Figure 3. Anterior projection of same case.

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Figure 4. Isodose lines around sources in Manchester ovoids, data obtained from computer. The dense white circle is radiopaque material in the Foley catheter, identifying floor of bladder.

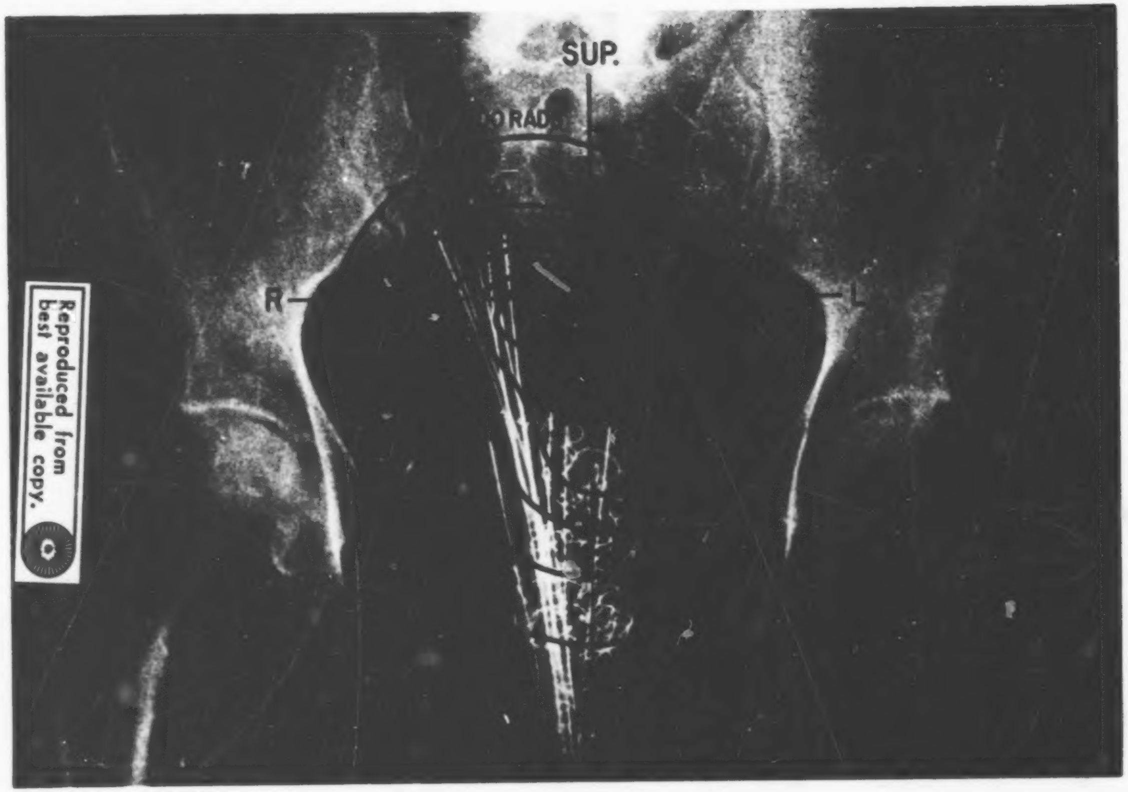

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Figure 5. Similar isodose lines about the sources in the uterine cavity and the vaginal fornices.

BRACHYRADIOTHERAPY OF ENDOMETRIAL CARCINOMA

Rado Poljansek, M.D., and Marjan Erjavec, M.D., Sc.D.

Intrauterine radium application is a simple and useful way to treat patients with endometrial carcinoma that, for one reason or another, is not amenable to radical surgery. It is also believed that this treatment, if applied before radical hysterectomy can increase the survival of patients and decrease the incidence of metastases.

The intrauterine devices used in the Institute of Oncology at Ljubljana, Yugoslavia, before 1963 were not satisfactory. Application of a single source into the uterus was insufficient, and residual or recurrent cancer frequently was observed following the insertion of multiple sources in a tandem arrangement.

After 1963, old devices were replaced by Heyman-type of applicators in all cases except those with a uterine canal 6 cm or less in length. Our 7-year data and method are summarized in tables 1 and 2.

The uterine cavity was packed with radium immediately after pathohistological verification of malignancy. Altogether, 3,600 to 5,400 mg hrs were administered in two or three insertions, depending on the size of the uterus and the depth of invasion. The sessions were one week apart.

After uterine treatment was completed, many patients also received vaginal irradiation by radium or iridium, up to about 4,000 rads in a single session.

For most of our patients, Heyman-type radium was the first treatment. Only 19 of the 105 cases received some other type of therapy (table 3).

In order to demonstrate the value of Heyman intracavitary radiotherapy, the patients selected were given no other treatment, and have had at least two years of followup. Their survival is shown in table 5.

Altogether, 46 of the 105 patients were treated only by Heyman radium packing: elderly women, or the very ill, or those who had advanced malignancy. Since these patients were not suitable for surgery, external irradiation, or chemotherapy, they represent the worst category.

The remainder of the patients were given various types of treatment additionally (table 4).

No lethal result due to Heyman uterine packing appears in our data.

Since we did not use this type of treatment before 1963, the 5-year followup can be shown only for a small group of 21 patients treated during the period of 1963-1965 (table 6).

Our data are too scant to be compared with results in larger institutions. We are convinced, however, that the survival rate has been increased by the introduction of the packing method. Moreover, the anticipated use of Simon's afterloading uterine applicators has aroused interest in the Gynecological Clinic at Ljubljana, and in the future we hope to get a greater portion of their patients irradiated preoperatively than occurred in the past.

Table 1. Packing of Uterus with radium (Heyman)

Site of Primary Cancer	No. of Patients
Endometrium	105
Cervix and ovaria	9
Nonmalignant conditions	14
TOTAL	128

Number of Insertions: 251
Doses of irradiation: 2-3 times 1,800 mgh
Insertions 1 week apart

Table 2. Endometrial carcinoma treated with radium (Heyman)

Histology	90 percent adenocarcinoma
Mean age	65 years
Nulliparae	13 percent
Uni/multiparae	53 percent
Unknown	34 percent

Table 3. Treatment of endometrial carcinoma prior to radium packing

External irradiation	7
Intracavitary radium	12
Probatory laparatomy	3
Diagncstic abrasion	105

Table 4. Treatment of endometrial carcinoma after radium packing

Radical surgery	26
Nonradical surgery	6
External irradiation	28
Intracavitary radium	19
Chemotherapy	10
Total patients treated	59
No treatment given	46
TOTAL	105

Table 5. Survival of patients with endometrial cardinoma treated only with radium packing of uterus

Survival	Total	Alive	Dead	Lost
4 years	6	3	3	-
3 years	26	9	14	3
2 years	38	14	20	4

Table 6. Survival of patients with endometrial carcinoma - radium packing combined with other therapy[1]

		Survival in years				
	Total	1	2	3	4	5
Number of patients	21	19	15	13	12	10
Percent of patients	100	90	71	62	57	48

[1] Patients with first treatment in 1963-1965

DISCUSSION

DR. KOTTMEIER: I would like to congratulate Dr. Simon for his very famous study, which we will certainly try in Stockholm. But I have two questions.

One involves my own experiments. When the late Professor Heyman treated carcinoma of the corpus, I was his associate. He had wire retainers fixed to the tubes. When I further developed the technique, it was almost impossible to remove the retainers from some uteri. Now if you pack the uterus and stretch the uterine wall, and you have to pack the lower corpus and the cervix with large capsules, is it always possible to remove the afterloading capsules?

DR. SIMON: Wise Dr. Kottmeier, you have struck my Achilles' heel. We have treated 22 patients. Much of our work has been feasibility studies, and in one patient the bonding of the plastic gave way. This patient was being irradiated preoperatively. We had inserted 11 capsules and removed the radioactive material, but left 4 afterloading capsules inside the uterine cavity, the tails having separated from the bulbous ends. In that instance the patient had fibroids and a very firm circuitous channel, and we did indeed pull the plastic tubes apart. We think we have solved this problem by improving the bonding of the tube to the bulbous end.

Technically speaking, I was pleased to see that you used Hegar dilators while some of your capsules were in place. In the first few patients we treated, we were unable to get enough capsules in the uterus until we began to use the tubes themselves as extra dilators. Having watched you work at the Radiumhemmet, and having learned how to put in Heyman applicators from Heyman himself in 1949, when you were Chief and he had just retired, I know that you could put those in much more efficiently than we amateurs.

INTERSTITIAL TECHNIQUES

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DEVELOPMENT OF AFTERLOADING IMPLANTS

Ulrich K. Henschke, M.D., Ph.D., David G. Mahan, Ph.D.,
Mattie J. Tabron, R.T., and Felix Mick, A.A.

The afterloading principle is a simple one; however, during introduction and removal one must be on guard against radiation exposure due to unsuitable designs of applicators, materials, instruments, and insufficient training and practice.

Good afterloading techniques completely eliminate radiation exposure in the diagnostic radiology department. They require little advance preparation, since only unloaded tubes and needles have to be available at the initial insertion. They can be kept sterile in the operating room ready for immediate insertion, thus the presence of radiation safety personnel in the operating room is not required. The radioactive sources can be ordered later and inserted after proper planning by the therapist at his convenience. This also provides for greater accuracy, since the position of the unloaded tubes can be palpated directly. The radioactive sources can be arranged or rearranged (if necessary) in an optimal pattern after studying dose distribution from roentgenograms of the dummy sources, and by direct dose measurements with a scintillation dosimeter after insertion of the radioactive sources.

In 1953 we described an afterloading technique for interstitial implants with gold 198 seeds. Since then the value of interstitial implantation for the cure and palliation of localized, unresectable cancers of low radioactivity has been well documented. However, because of organizational problems (source supply, instrumentation, radiation protection, expenses, training, etc.) interstitial implantation is underused in cancer management.

At Howard University, we are trying to perfect a pilot facility which we hope will lead to wider use of interstitial implantation and better results. Our system is based on a single iridium 192 source of very small size, used in varying numbers and arrangements for removable implants, intracavitary and surface applications; it can also be used directly for permanent implants.

Iridium 192, developed for interstitial implantation by Henschke and Mahan in 1954, was chosen because it has proven as the best all around radioisotope for implants. It is easily produced in smallest sizes in reactors of moderate neutron flux (due to its large neutron cross section of 750 barns); its primary beta particles (670 KeV maximum) are sufficiently absorbed by 0.2 mm of stainless steel; its gamma radiation (380 KeV average with a half-time of 74.5 days) is convenient for removable as well as for permanent application; and it is most economical.

A single type source of very small size was chosen because it can be mass produced, stored, shipped and handled much more easily and economically than larger sources. Our new Howard University Type HU-I source has an overall length of 2.5 mm, and a diameter of 0.5 mm. It consists of a fine iridium 192 core (0.1 mm diameter) surrounded by two layers of stainless steel.

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PERMANENT AND REMOVABLE IRIDIUM 192 IMPLANTS:

TECHNICAL MODIFICATIONS IN LJUBLJANA, YUGOSLAVIA

Marjan Erjavec, M.D., Sc.D.; Primoz Cevc, B.S.;
and Rado Poljansek, M.D.

Iridium 192 wires for temporary implants in tumors have been used in conjunction with afterloading techniques in the Institute of Oncology, Ljubljana, since 1963, and since 1969 we have also used iridium spheres for permanent implantation.

The techniques employed for iridium wires (figure 1) are basically those suggested by Henschke and Pierquin. By means of ordinary hollow needles, teflon tubes first are introduced into the tumor. The sources for subsequent loading, however, have been slightly changed. Instead of plastic material containing platinum-covered iridium wires, we use stainless steel tubes 0.3 mm in outer diameter (figure 2). The active part is 2-6 cm long, and contains a platinum-iridium wire 0.1 in diameter. The inactive part is 5 cm long, contains no iridium, and is slightly angled toward the active end. It also bears an identification mark that facilitates handling of the wire.

A set of about 30 sources of suitable lengths is prepared in advance and sent to the reactor for activation. After a few days of cooling down the short-lived parasite radioactivity, a linear strength of about 3 mCi/cm is achieved.

In comparison with iridium sources currently used in Europe, the advantages of these wires are as follows:

- They are reusable, and need no rearrangement when active;
- They are tiny but firmer than plastic material, easy to introduce, yet flexible enough to bend with the tissues;
- The material is very cheap and can be discarded after decay.

The same wires, bent into entire-length-active hairpins, are used in conjunction with the semi-afterloading technique introduced by Pierquin and Chassagne (figure 3).

Iridium 192 spheres 0.8 mm in diameter are produced by SORIN, in Italy. For permanent implantation of these spheres we use ISOFIX equipment developed by Nervi and Gallo. First, long hollow needles are inserted into the tumor in order to secure a suitable distribution. Subsequent disposition of the spheres into the tissues is performed by means of the original implantation instrument.

Radioactivity to implant being low (mostly about 3 mCi), we did not insist on the sophisticated but somewhat bulky original unit for dispensing the spheres. Instead, we mounted a handy magazine containing up to 45 spheres on the side of the implanting instrument itself. A turn-button mechanism ejects the spheres, one by one, into the body of the instrument, enabling implantation with sufficient accuracy. This instrument has proved to be extremely convenient and helps to speed up the period of active intervention, thereby reducing unnecessary exposure of personnel to almost negligible amounts.

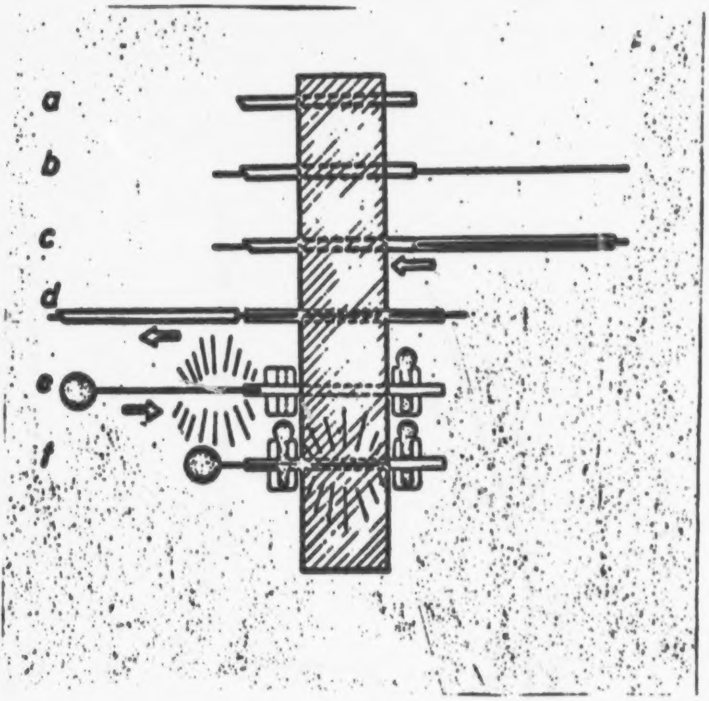

Figure 1. Implantation of tumor with iridium 192 wire by technique of Pierquin and Henschke. Hollow steel needle (a) is inserted into tumor, and Teflon tube containing dummy wire replaces hollow steel needle (b, c, d). Finally, iridium 192 wire is inserted (e) and fixed (f) in tissue.

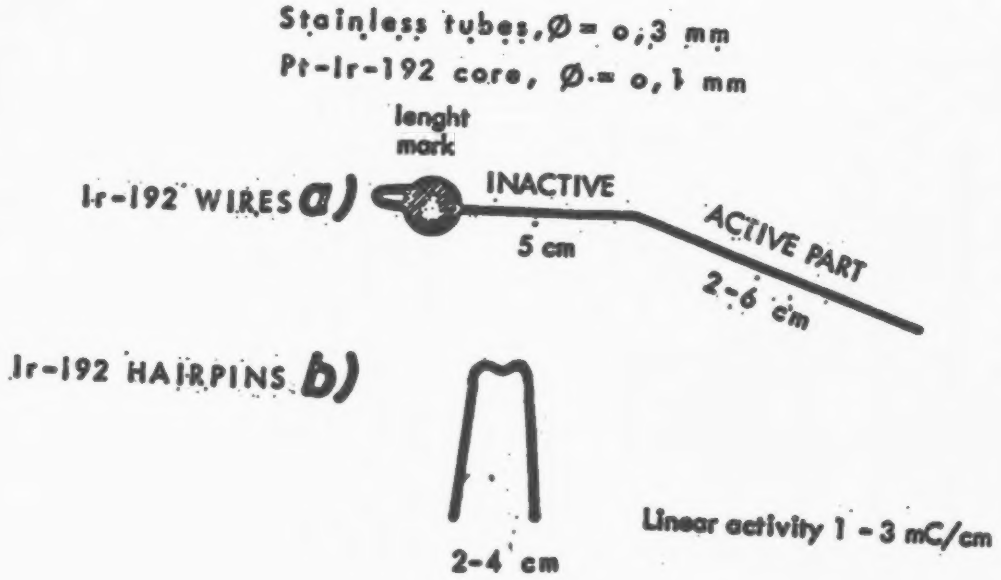
Stainless tubes, Ø = o,3 mm
Pt-Ir-192 core, Ø = o,1 mm
lenght mark
Ir-192 WIRES a)
INACTIVE
5 cm
ACTIVE PART
2-6 cm
Ir-192 HAIRPINS b)
2-4 cm
Linear activity 1 - 3 mC/cm

Figure 2. Modified iridium 192 wire in stainless steel tube 0.3 mm in outer diameter. Active source is 0.1 mm diameter.

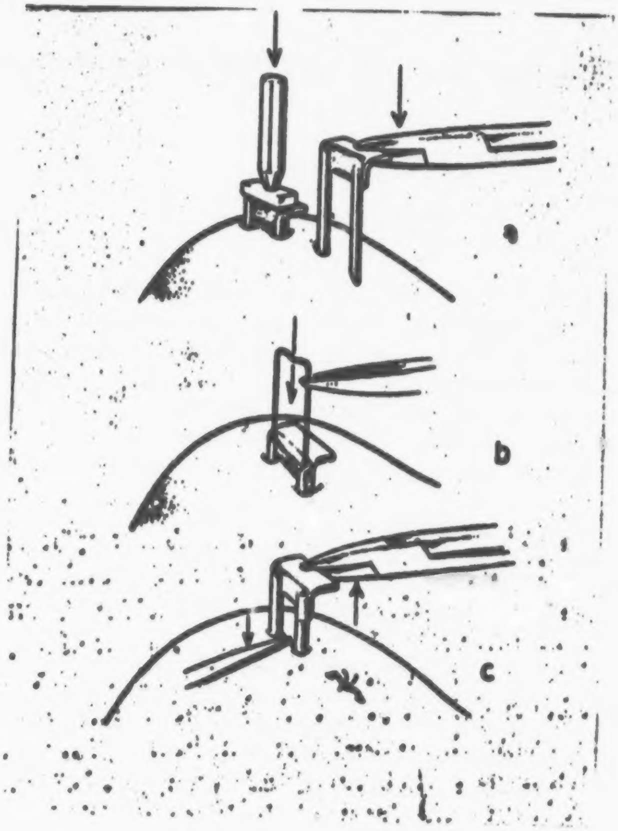

Figure 3. Same modified wire used in Pierquin hairpin technique for implantation of cancer of tongue.

INTERSTITIAL RADIATION USING IODINE 125 ENCAPSULATED SOURCES

Basil S. Hilaris, M.D.

Encapsulated iodine 125 sources were introduced for the first time at Memorial Hospital in 1965 as a substitute for high energy gamma emitters, to eliminate or substantially decrease radiation exposure from an interstitial implant (1). Many of the earlier problems of fabrication of the iodine seeds have been solved in the intervening years, and they are now commercially available at a price comparable to that of other radioactive sources.

The biomedical program to study the iodine seeds, undertaken with support of the Bureau of Radiological Health, U. S. Public Health Service, was divided into three identifiable areas: (1) Radiation exposure, (2) radiation dosimetry, and (3) clinical trials.

The first objective, to eliminate or reduce radiation exposure, was achieved. The use of iodine 125 seeds has reduced the radiation exposure to such a low level that no significant radiation is now recorded on the personnel film badges. With the use of radon 222 and gold 198, film badges often showed undesirably high exposure (figure 1).

The second objective, that of the dosimetry, also was successfully completed. G. Holt recently reported the work done in this respect by the Physics Department at Memorial Hospital (2). The absorbed dose (K) at a point in the absorbing body was determined to be 1.7 rads per mCi hour at a distance of 1 cm. Using this K value, the total dose delivered at 1 cm from an iodine 125 seed left in place for total decay is calculated to be 3,525 rads per mCi. This compares with 1,050 rads per mCi for radon 222, or a ratio of 1:3.4. It does not take consideration any difference in biological effects due to marked difference in half-life. However, one would conclude that the required activity per seed in an interstitial implant of iodine 125 seeds should be less than that required if radon seeds were used.

This work was supported by PHS Grant EC 00113 and by Contract No. PH 86-66-132 from the Bureau of Radiological Health, Rockville, Md. 20852.

Radiation dose distribution within the implanted regions is computed by means of the Memorial Midas computerized dosimetry system. Complete isodose distributions are computed for each patient who receives an interstitial implant. The seeds are localized according to the Memorial orthogonal-stereo method.

Figure 2 shows an example of a matrix in the midplane of a lateral projection. Isodose curves indicating various dose levels are shown. An explanation of the actual dose levels is in the upper left corner. This matrix is magnified by a factor similar to the radiograph utilized for the calculations. The main anatomic features and the radioactive seeds are traced on top of the matrix, so that printout and film are correlated. In addition, the same program provides the tissue volume in cubic cm that has received the corresponding minimum total dose.

A study also was undertaken to compare isodose distributions within lesions with iodine 125 seeds to those obtainable with radon seeds. The comparison disclosed that by and large distribution within the implanted region did not differ greatly for radon and iodine 125 seeds. Outside of the implanted volume, however, there was a marked fall-off in radiation dose when iodine 125 seeds were used (3).

The third objective, that of clinical trials, will be the main subject of this presentation. Figure 3 is a photograph of the complete kit for permanent interstitial implantation developed specifically for iodine seeds. It includes besides the "gun" a set of 15 hollow, 17 gauge stainless steel needles used during the first step of afterloading technique; a stainless steel ruler subdivided into centimeters; and five magazines, each containing 10 low energy iodine 125 seeds. These components are mounted on a removable stainless steel base that can be autoclaved and kept sterile in the operating room prior to the implantation.

One of the key problems in using low energy iodine 125 seeds was determination of the optimal dose. In 1968, after reviewing implants with iodine 125 up to that time, we arrived at an estimate of the optimal dose for permanent implant volumes and presented this in the form of a curve. Figure 4 shows the estimated optimal doses for iodine 125 implants (dotted line) plotted against the implanted volume. For purposes of comparison, a similar curve for radon 222 implants is shown (4, 5). In this curve, 16,000 rads is the optimal dose for medium sized implants only. For smaller volumes, much higher doses are considered safe and essential in the attainment of optimal control. On the other hand, for large volumes the optimal dose falls below 16,000 rads. There are other factors, of course, that influence optimal dose -- such as previous radiation, radiosensitivity of the tumor, oxygenation, etc. -- for which allowances should be made.

Calculation of the required activity for each implant is determined by the "average dimension" system, which we had used for years with Dr. Henschke to determine activity for implants with high energy gamma emitters (5). Figure 5 illustrates the principle of this system. The three dimensions of the implanted volume must first be determined, and this should be done after the insertion of the needles. Two dimensions can be measured directly with a ruler; the third dimension also is determined easily, since all needles are 15 cm long. Let us assume that the three dimensions are 5, 4, and 3 cm. The average dimension is then

$$\frac{5 + 4 + 3}{3} = \frac{12}{3} = 4 \text{ cm.}$$

It is simply multiplied by an empirical factor of 5 for iodine 125 seeds. This gives 20, the recommended activity of iodine 125 in mCi for this implant, and results in the optimal dose according to the previously mentioned curve. If the implant is a single plane, the third dimension is taken as zero. This method of calculation applies to a cube or rectangular-shaped volume. If the volume is cylindrical, 10 percent has to be deducted; and if the volume is spherical, 20 percent is deducted. The number of seeds is found by dividing the total millicuries by the average activity of the seeds (20 ÷ 0.5 = 40 seeds). A detailed mathematical analysis of this study was published in 1968 (6).

Table 1 lists the location in which permanent implants with iodine 125 seeds were used. From December, 1965, to December, 1970, a total of 300 implants were performed in 277 patients. About 80 percent of these patients with iodine 125 implants had advanced tumors previously treated by surgical excision, external radiation, or a combination of both. No long survivals were expected in this group. Tumor regression, therefore, was the only useful parameter to judge the efficacy of the treatment. Regression did not depend on the location, size, or histology of the tumor; it was dependent, however, on total dose and proper implantation of the tumor.

Figure 6 shows an example of a permanent implant in a patient with metastatic neck nodes, previously treated with 4,000 rads by means of the cobalt teletherapy unit. Two residual nodes in the right neck, the largest measuring 4 x 3.5 x 1.5 cm, were implanted with iodine 125 seeds (11.7 mCi and 5 mCi, respectively). The minimum tumor dose was 16,000 rads. The graph on the left shows the pattern of regression for both nodes. Complete regression was achieved within one month following implantation. The photograph on the right shows the patient 5 months after implantation, with no evidence of recurrence in the neck.

Permanent interstitial implants with iodine 125 seeds proved to be of particular value in cancer of the lung and prostate. Table 2 gives the number of interstitial implants from 1955 through April, 1970, in 305 patients with cancer of the lung proven unresectable at thoracotomy. During this period various radionuclides were implanted, using afterloading techniques (7). Since September, 1969, only iodine 125 seeds were utilized for this type of implantation.

Figure 7 shows the percent survival by year, according to the Berkson-Gage method, for the implanted patients. For purposes of comparison, patients are divided into three groups. In one group, radionuclides with high energy and short half-life were used (radon 222 and gold 198). A total of 211 patients had implants in this category from 1955 through 1968. Gold seeds were used only during the years 1962 and 1963. The second group includes 68 patients in whom radionuclides with high energy and long half-life were used (iridium 192). These implants were carried out from 1956 through 1961. Finally, the third group includes 26 patients implanted with radionuclides of low energy and long half-life (iodine 125) from 1966 through April 1970. The corresponding 5-year survival rates were 5, 2.8, and 9 percent. There is no statistically significant difference in these figures.

Iodine 125 emerges, therefore, as a radionuclide with definite advantages for permanent implants because of its low energy, resulting in negligible exposure to personnel involved and lack of any need for precautions and restrictions to the patient following implantation. If there is any selective effect on the cancer cells due to the low dose rate, it is not evident as yet. Detection of any such effect, if present, would require larger samples of patients than those presently available.

The second area where interstitial implantation appeared to be of value, using the low energy radionuclides, is in cancer of the prostate. The interstitial implantation of encapsulated sources has distinct advantages, when compared with external radiation therapy in the treatment of this malignancy (figure 8). The two cross sections of the pelvis at the level of the prostate show the same primary prostatic cancer. The drawing on the left is an example of an optimum setup with external radiation therapy. Using the linear accelerator and 360 degree rotation, it is possible to deliver 6,000 rads to the tumor-bearing area in about 6 weeks. The adjacent rectum and bladder will receive a dose in the range of 4,000 to 4,500 rads in the same period. The drawing on the right is an example of dose distribution for an interstitial implant with iodine 125 seeds in the same situation. Comparison of these isodose curves demonstrates the following advantages of interstitial implantation:

1. Tumor dose with an iodine implant is much higher: 16,000 rads vs. 6,000 rads with external radiation.

2. Localization is more precise, and the dose distribution can easily be adapted to the irregular tumor shape.

3. The dose to the bladder and rectum is in the range of 4,000 rads, but it is delivered over a longer period (approximately 1 year as compared with 6 weeks when external radiation is used).

4. Finally, the time required to carry out treatment is much shorter. External radiation therapy extends over a period of 6 to 7 weeks; with a permanent implant the entire treatment is completed at the time of implantation.

Figure 9 illustrates the retropubic approach for interstitial implantation of the prostate. This approach is preferred because it permits complete mobilization of the prostate, allowing more accurate determination of the tumor extent, especially laterally. The nodes can be inspected, and extraperitoneal node dissection performed. More adequate manipulation is afforded by a catheter in the bladder outlining the urethra, and by inserting the operator's finger into the rectum.

Figure 10 is an example of such an implant. The radioactive seeds (light colored dots) indicate the implanted volume, and are utilized to determine the target area. The isodose curve encircling these seeds on the left radiograph is the minimum tumor dose. In this example it is 16,000 rads (darker line) as recommended by the average dimension system, given to 22 cc of tissue. The dose falls off rapidly, becoming approximately 4,000 rads at the level of the rectum. The radiograph on the right belongs to the same patient and was taken 6 months later. The radioactive seeds are closer together, indicating regression of the tumor.

CONCLUSIONS

Five years after initiation of the program to study low-energy iodine 125 seeds, the following conclusions can be drawn:

Optimal activity of radioactive sources is between 0.4 and 0.6 mCi; optimal spacing of the seeds is 1 to 1.5 cm, the greater distance being used for seeds in the center of the implanted volume.

Minimum tumor dose of about 16,000 rads is required for optimal effect in the average implant (15-85 cc or 2.5-5.4 cm average dimension). This dose is well tolerated and without undesirable side effects.

Implanted tumors receiving the above dose will show at least 50 percent regression by the fourth week after implantation (a tumor dose of approximately 4,000 rads).

These tumors usually have completely regressed by the end of the first half-life of the iodine 125 (60 days). Cancer cells, however, may be seen for at least two more half-lives (180 days), although they apparently are not viable. Biopsy therefore is not recommended until 6 to 8 months after implantation, so long as there is no evidence of tumor activity.

Additional radiation therapy, if possible, is recommended in all patients with a tumor size less than 4 cm who received, by the iodine implant, less than 8,000 rads during the first half-life of the isotope, or 16,000 rads in total decay. Our practice has been to supplement as much external radiation therapy as is required to bring the combined dose from implant and external radiation to 8,000 rads during the first half-life. We usually add this supplementary irradiation 3 to 4 weeks after implantation.

The original objectives relative to the iodine 125 program have been achieved. Radiation exposure has for all practical purposes been eliminated; the basic dosimetric program has been developed; and accumulated clinical experience shows that low energy radionuclides have the same effect on normal tissues and neoplastic tumors as the high energy gamma emitters used previously.

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Table 1. Permanent interstitial implants with iodine 125 sources (Dec. 1965 through Dec. 1970)

Site	Number of implants
Intraoral	33
Superficial: Neck	94
Other	97
Intrathoracic	61
Intraabdominal	75
Total	300

Table 2. Interstitial implantation at thoracotomy unresectable cancer of the lung (1955 - 1970)

Radionuclide	Number of patients
Radon 222	197
Gold 198	14
Iridium 192	68
Iodine 125	26
Total	305

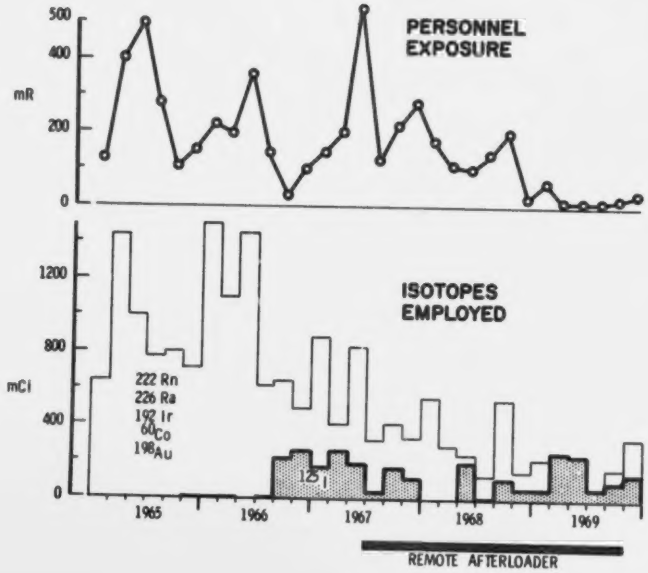
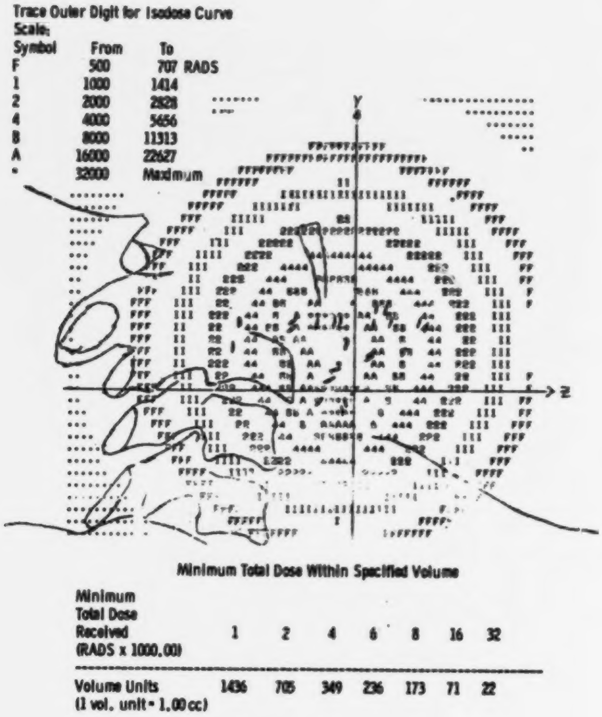


Figure 1. Reduction of radiation exposure (1965-69) as the result of use of iodine 125.



Trace Outer Digit for Isodose Curve
Scale:

Symbol	From	To
F	500	707 RADS
1	1000	1414
2	2000	2828
4	4000	5656
8	8000	11313
A	16000	22627
*	32000	Maximum

Minimum Total Dose Within Specified Volume

Minimum Total Dose Received (RADS x 1000.00)	1	2	4	6	8	16	32
Volume Units (1 vol. unit = 1.00 cc)	1436	705	349	236	173	71	22

Figure 2. Matrix of radiation dose distribution in the midplane of a lateral projection.

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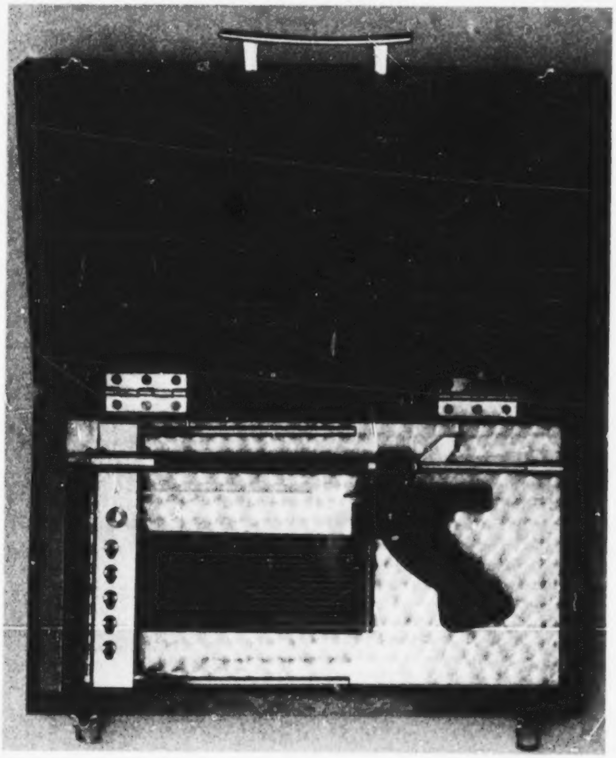

Figure 3. Kit for permanent interstitial implantation with iodine 125 seeds.

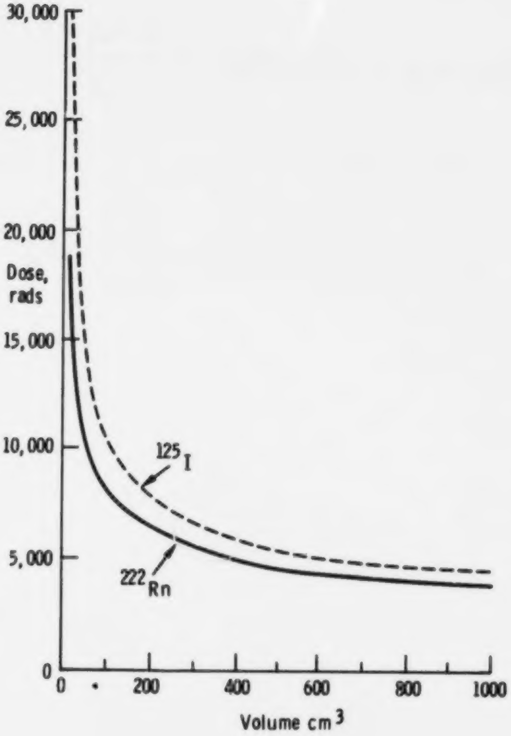

Figure 4. Estimate of the optimal dose for permanent implant volumes.

$$\text{Average Dimension} = \frac{5+4+3}{3} = 4\,\text{cm}$$

$$MC_1 \text{ Iodine 125} = 4 \times 5 = 20$$

$$\text{Number of Seeds} = \frac{20}{0.5} = 40$$

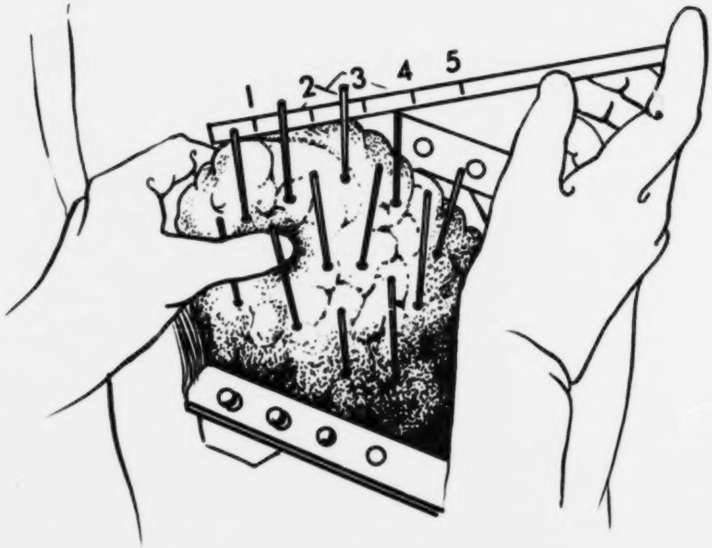

Figure 5. Calculation of iodine 125 activity.

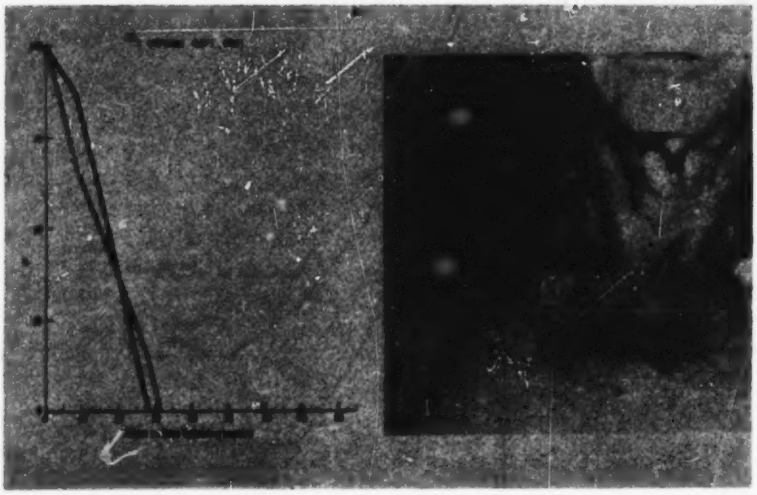

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Figure 6. Pattern of regression following permanent iodine 125 implant in patient with metastatic neck nodes. Photo shows patient 5 months after implantation.

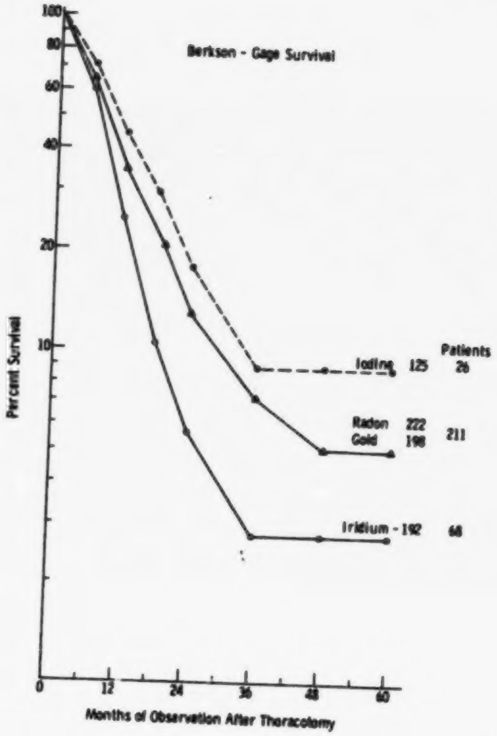

Figure 7. Interstitial implantation unresectable carcinoma of lung (1955 - 1970)

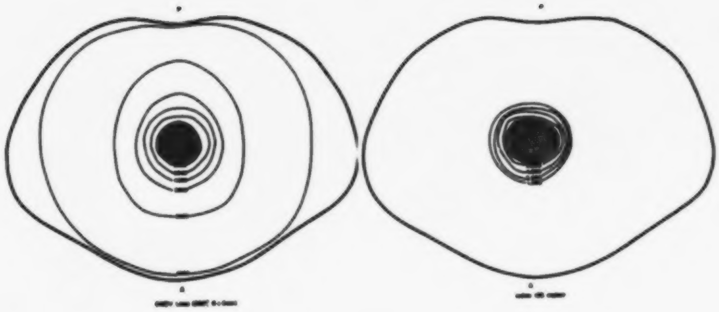

Figure 8. Dose distribution in primary prostatic cancer using external radiation (left) and interstitial implantation with iodine 125 seeds (right).

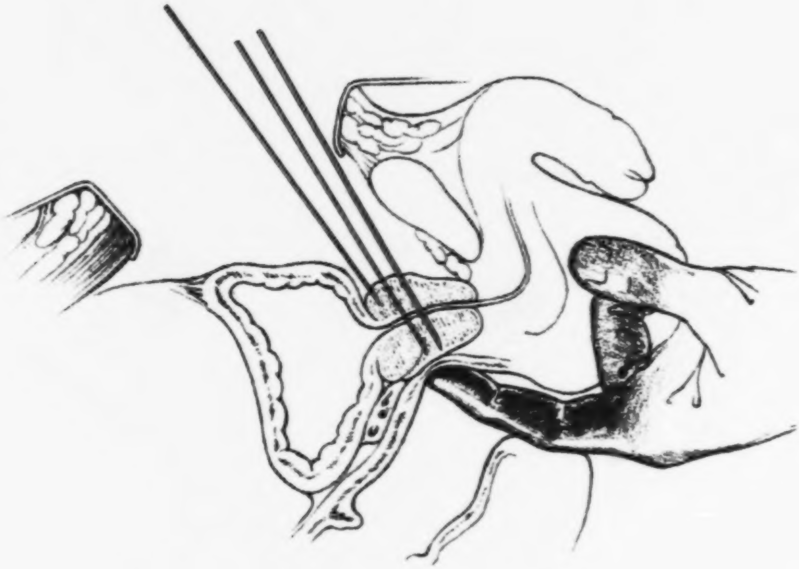

Figure 9. Retropelvic approach for interstitial implantation of the prostate.

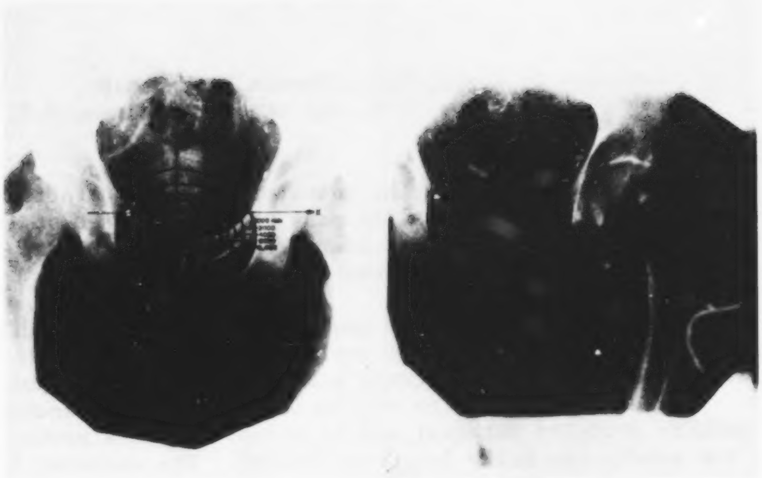

Figure 10. Interstitial implantation of the prostate. The isodose curve (left) shows minimum tumor dose. Radiograph (right) 6 months later shows regression of tumor.

A SIMPLE AFTERLOADING NEEDLE TECHNIQUE

Lawrence C. Roach, M.D., Norman Simon, M.D.,
Sidney M. Silverstone, M.D. and Eugene Friedman, M.D.

Radium needles have been the mainstay in the interstitial implantation of malignant tumors for many years. Because of its limitations, there has been constant search for a substitute as effective as radium but without its drawbacks.

The disadvantages of radium needles lie in their rigidity, thickness, possible breakage and explosion, leakage, and the heavy shield they require. The rigidity makes implantation around a curved surface difficult. The thickness, necessary to enclose the low specific activity material and to screen out beta particles, makes the needle too bulky for afterloading. The operator implanting radium needles must work rapidly because of radiation exposure. Along with the fear of radiation exposure is concern with breaking a needle and spilling its long lived contents, contaminating operating rooms and even buildings.

These difficulties have led to the use of fewer interstitial implants in cancer management, and to fewer radiotherapists trained in this useful method for the treatment of localized cancer. Many have abandoned this form of treatment in favor of external beam therapy, despite the inefficiency of treating an excess of normal tissue with beam therapy.

There is a need for a radium substitute that can be afterloaded and will have greater flexibility than radium. Also, afterloading will increase the accuracy of placement of the radioactive material. In 1958 Henschke spearheaded the search for such a substitute. He proposed a system based on an array of seeds of metallic iridium 192 in a plastic tube for afterloading removable implants (1-3).

Others, including Simon in our hospital, adapted Henschke's technique for the implantation of tumors of the oral cavity, neck, breast, and pelvis (4, 5). The flexibility of the method allowed implantation of tumors prohibited by the rigidity of the classical radium needles. However, iridium 192 became unobtainable commercially, its shelf life was limited, delivery problems developed, and the plastic holding the tube became brittle from the effect of radiation. Users of iridium 192 had to go back to radium, or develop more practical methods of their own.

Suit made rigid needles for afterloading in 1960, but his system for afterloading interstitial implants has not become as popular as that for afterloading cervix system (6).

Tantalum 182 has been used in Britain and Canada by a technique whereby tantalum 182 wire is introduced percutaneously through a guiding-needle system (7). Cobalt 60 has been fashioned into needles like radium needles and is commercially available, but not for afterloading.

We have adapted the common intracath for interstitial implants. This is a device familiar to all physicians, easily manipulated without special training, and incidentally almost exactly the size of the traditional radium needles. Most important, they can be afterloaded with miniaturized radioactive sources (figure 1).

In the early development of this method we used the available thin sources of cobalt 60 wire. We now are supplied with cesium 137 sources of similar size. They are comprised of a 0.7 mm cylinder of Vycor glass containing cesium 137 annealed within it and welded into the lumen of 18 gauge needle tubing. In the manufacture of these sources, the cesium 137 in solution is incorporated into porous cavities in Vycor glass rods. Each cavity is 25^{o}A in diameter. The rods then are heated to seal the radioactive material within the glass. The Vycor glass rod is slipped into closed end steel tubing, and welded over.

We have treated various types of tumors with these sources, demonstrating the applicability of the method.

CASE 1

A 57-year-old woman had a 3 cm mass in the upper outer quadrant of the left breast. X ray showed metastases of the spine. Needle biopsy was reported as adenocarcinoma. While she was receiving cobalt 60 teletherapy to the spine, it was decided to implant the breast lesion with the afterloading technique. The patient was premedicated with demerol 100 mg and compazine 10 mg I.M., and taken to the radiotherapy department where an area 4 by 4 cm containing the tumor was outlined. The points where we planned to introduce plastic intracath needles were infiltrated with 2 percent zylocaine. The five catheter needles were placed parallel to each other and in a single plane so arranged that the activity extended beyond the tumor sufficiently to make crossing of the ends unnecessary (figure 2).

The plastic tubes were afterloaded with thin cobalt 60 needles, 18 gauge in diameter and 4 cm in active length (figure 3). The five needles, each containing 4 mCi of cobalt (32 mg of Ra equiv.), were left in for 44 hours to give an estimated minimal dose of 4,500 rads at 0.5 cm from the plane of the implant. A sixth Angiocath needle containing an array of tiny lithium fluoride rods was placed diagonally across the irradiated field for direct measurements (figure 4).

The patient tolerated this procedure well, and was discharged the same day the needles were removed. A follow-up picture of the breast 10 days later showed a brisk erythema at the sites of the needle implant (figure 5). Now 10 months later, the breast tumor is palpable but the osteoblastic metastases continue to increase.

CASE 2

A 75-year-old woman has bilateral breast carcinoma. The left breast contained an ulcerated mass 8 cm in diameter in the upper outer quadrant, fixed to an axillary mass of nodes. The right breast contained a similar but smaller ulcerated mass, 4 cm in diameter, located in the upper outer quadrant and extending into the axilla. Referred for radiotherapy by the surgical consultant, she was started on a course of cobalt teletherapy to both breasts. During the course of therapy she fell out of bed and broke her leg.

At the time of surgical fixation of the fracture both breasts, now greatly reduced in size, were implanted using an afterloading technique. There was no radiation exposure to operating room personnel. As in the previous case, the plastic tubes later were afterloaded with cobalt needles for an additional dose of 2,000 rads to each tumor.

The needles and intracaths were removed at the patient's bedside without discomfort. The masses continued to regress in later weeks.

CASE 3

A 54-year-old man was treated by external irradiation and multiple operations, including radical maxillectomy, for local recurrences of a cylindroma of the right maxilla. A further recurrence now involved the right soft palate with the antral defect, and extended posteriorly to the pterygoid fossa.

All tumor was excised, except for cancer adherent to the posterior antral wall. The unresectable tumor was implanted with four intracath plastic tubes placed parallel 1 cm apart in a single plane (figure 6). The tubes were maintained immobile with xerofoam gauze packing (figure 7). Catgut sutures were used as a bridge to prevent the packing from dropping out the mouth (figure 8). The hubs of the intracath needles remained exposed for afterloading with radioactive needles. Four cobalt 60 needles similar to those used in Case 1, were afterloaded. The dose was 750 mg hours, equivalent to 4,500 rads on the surface of the recurrent tumor.

Nine months later there was no evidence of recurrence.

CASE 4

A 55-year-old woman was admitted to the hospital for resection of a recurrent mixed tumor of the parotid gland. En block resection of the tumor was performed, but the tumor extended behind the upper end of the sterno-mastoid muscle and invaded the cartilage of the external auditory canal.

The area of residual disease was implanted with three afterloading intracath needles by the attending surgeon. Again, there was no radiation exposure to operating room personnel. The wound was closed and dressed with the hubs of the needles projecting through the dressing for ease of afterloading with radioactive material. The position of the Angiocaths was determined by x ray (figure 9). The needles later were afterloaded at the patient's bedside, and left in 35 hours for an estimated dose of 2,000 rads.

CASE 5

A 55-year-old woman presented with carcinoma of the vulva. An ulcerated tumor 5 by 5 cm involved the left labium minus, while a similar but smaller lesion 2 cm in diameter was present on the right labium minus. Both lesions were squamous cell carcinoma. There was no evidence of metastasis.

Under general anesthesia, with the patient in the lithotomy position, the left labium minus was implanted with three Angiocaths placed vertically 1 cm apart, their ends crossed by a fourth Angiocath which lay horizontally at the lower margin of the lesion. Both labia minora were sewn together so that the smaller lesion on the right labium was brought in close proximity to the plane of the needles. The procedure lasted about 30 minutes and there was no radiation exposure to operating room personnel. The Angiocaths later were afterloaded at the patient's bedside with four cobalt needles. In 48 hours a dose of 5,000 rads was delivered according to the Paterson-Parker rules. Subsequently, a node 1 cm in diameter appeared in the left inquinal region, and a node dissection was planned.

CASE 6

A 69-year-old woman presented with an ulcerated squamous cell carcinoma of the lateral surface of the tongue, at the junction of the middle and posterior thirds, measuring 2 cm in thickness and 4 cm in its axial diameter. External cobalt teletherapy was administered for a tumor dose of 4,300 rads in 4 weeks. The residual measured 1 by 1 by 1.5 cm, and she was admitted to the hospital for implantation of the residuum by the afterloading technique.

Under general anesthesia, an area 3 x 2 cm was implanted with Angiocath needles placed 1 cm apart, sutured in situs, and afterloaded with cobalt 60. In 24 hours a dose of 2,000 rads at 5 cm from the plane of the implant was given.

Discussion

These six cases were presented to show the feasibility of using miniaturized radioactive sources in interstitial implantation, in place of radium.

With substitutes for radium comes easier protection; and with miniaturization comes ease of handling, ease of afterloading, and universality of use. Different types of tumors can be irradiated with the same radioactive needles, using the same afterloading technique.

Unlike radium, cobalt and cesium, because of their high specific activity, can be miniaturized. Cesium has the added advantage of a long half-life (26 years) and a gamma ray energy (.66 MeV) that presents less of a problem of protection and storage than either radium or cobalt 60.

Case 1 and 2 demonstrate the ease of the method and its convenience. The entire procedure, performed during one of the patient's routine visits for external therapy, was no more traumatic than injection with an 18 gauge needle. It prevented further trips for a 3 to 6 weeks course of teletherapy, and spared the operating room time and expense of mastectomy in the women with bony metastases (Stage IV).

Cases 3 and 4, involving close cooperation of surgeon and radiotherapist, solved a problem that is often encountered: recurrent residual disease in an area previously treated by radical surgery and/or radical external radiotherapy. It appears to be a reasonable method for treating deep, nonresectable residual masses.

Cases 5 and 6 (the tongue and vulva) are classical examples of the implantation employed in most radiotherapy centers. Our afterloading technique with radioactive needles is a modification that brings with it total protection to operating room staff, and ease and accuracy to the radiotherapist.

Summary

A simple technique for afterloading radioactive needles for interstitial irradiation has been described, and 6 cases presented.

The ease and advantages of afterloading miniaturized cesium 137 needles are outlined.

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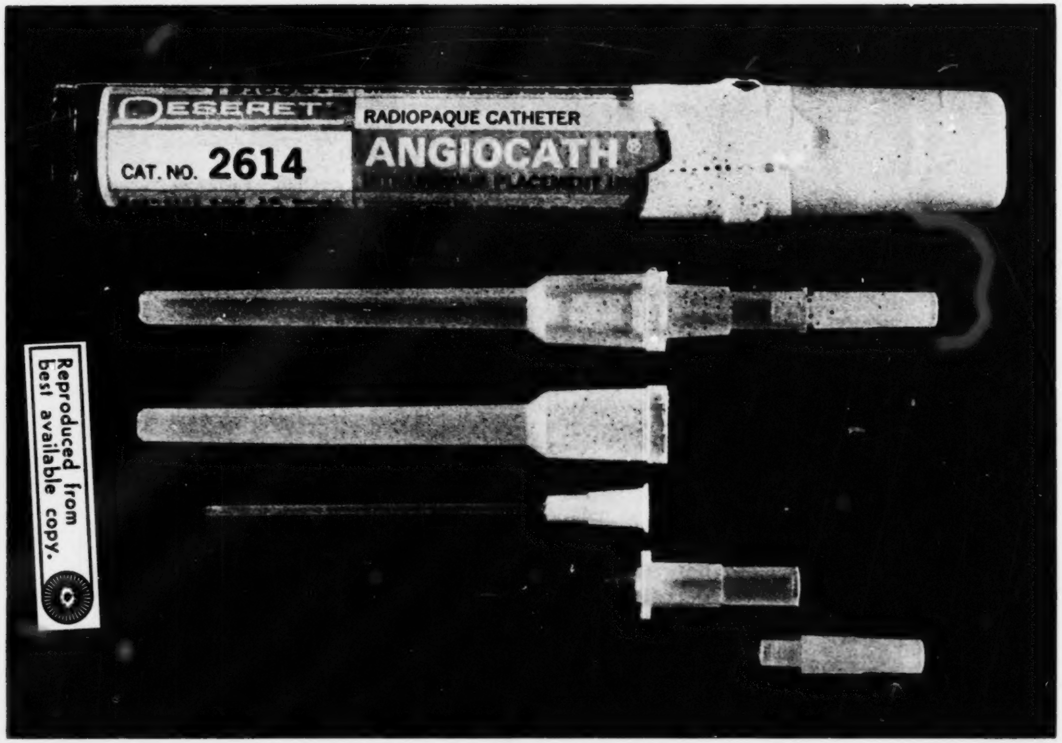
DESERET
RADIOPAQUE CATHETER
ANGIOCATH®
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Figure 1. Commercially available angiocath.

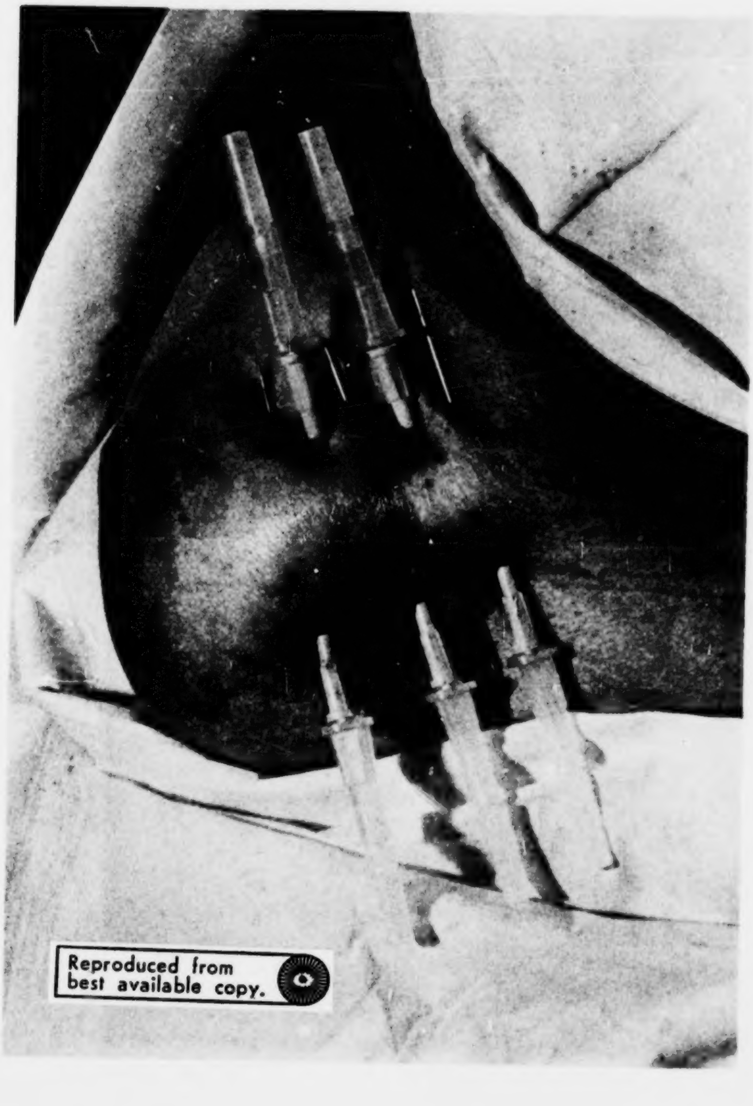

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Figure 2. Array of five catheters in breast.

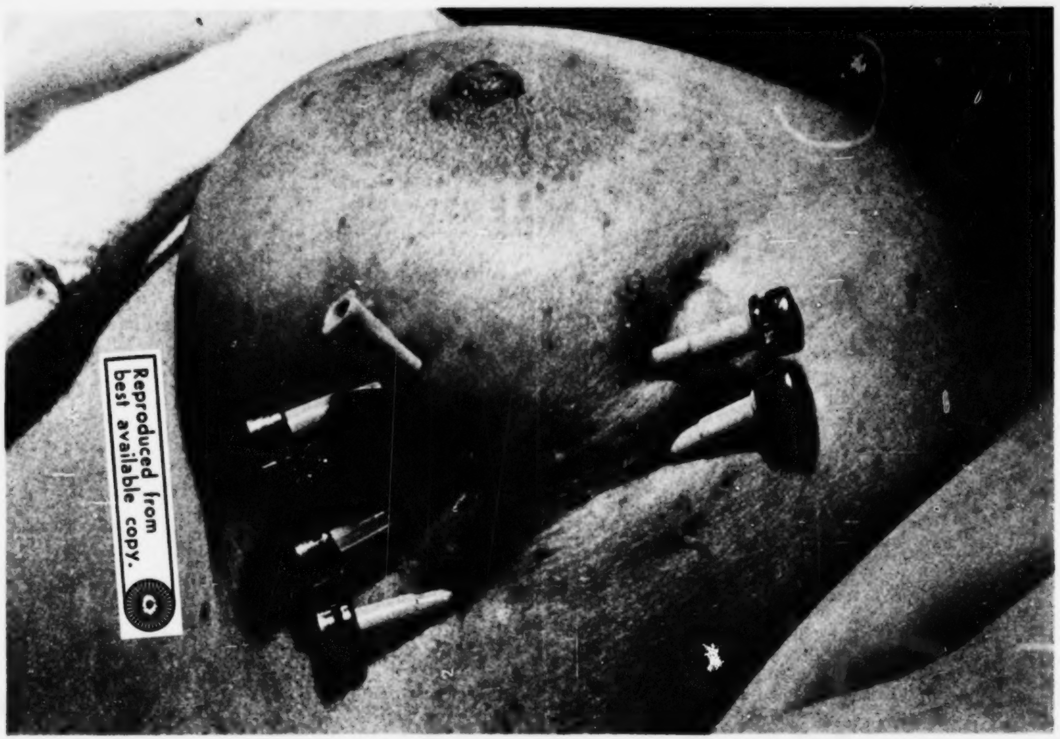

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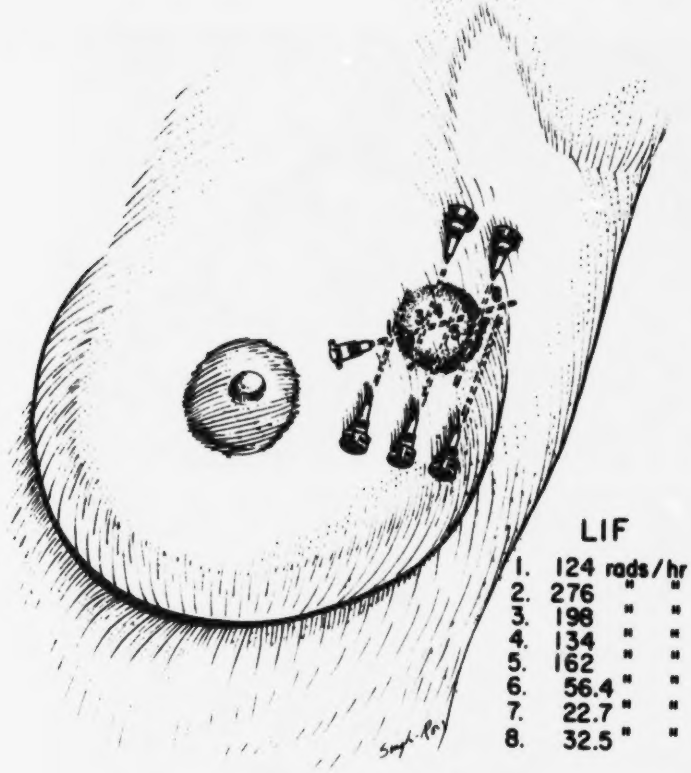
Figure 3. Cobalt 60 needles in catheters.



LIF
1. 124 rads/hr
2. 276 " "
3. 198 " "
4. 134 " "
5. 162 " "
6. 56.4 " "
7. 22.7 " "
8. 32.5 " "

Figure 4. Placement of six angiocath needles, one containing LiF dosimeters.

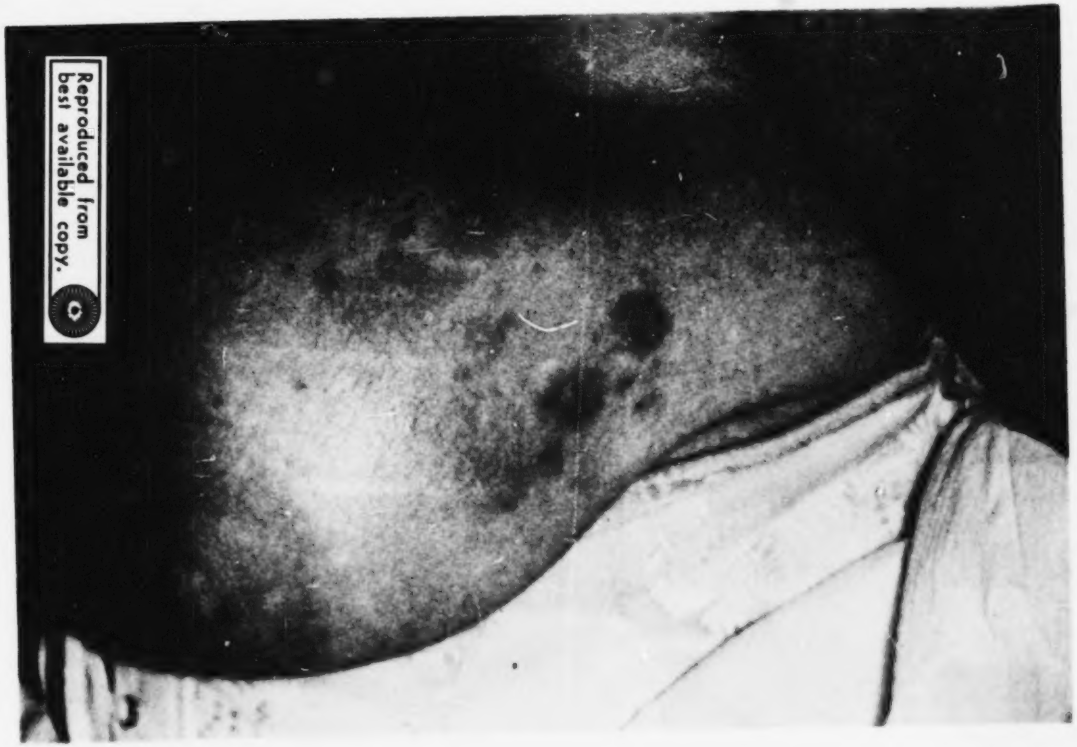


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Figure 5. Reaction at site of implant.

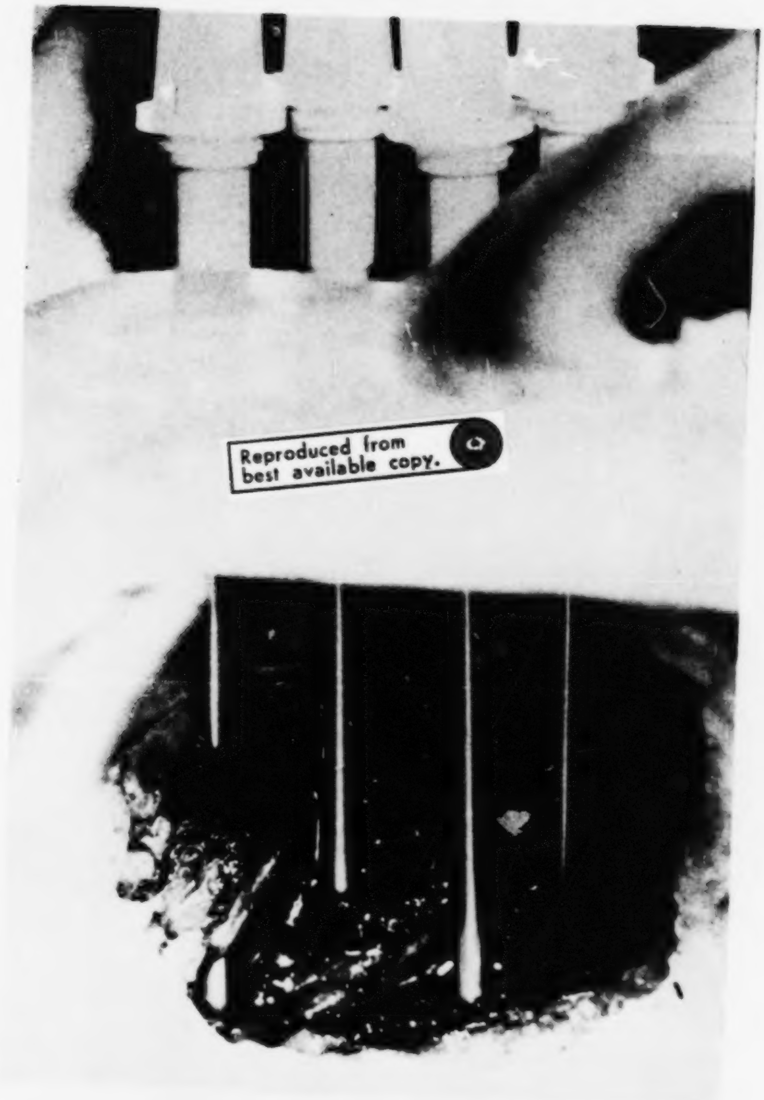

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Figure 6. Plastic tubes at base of unresected tumor of antrum.

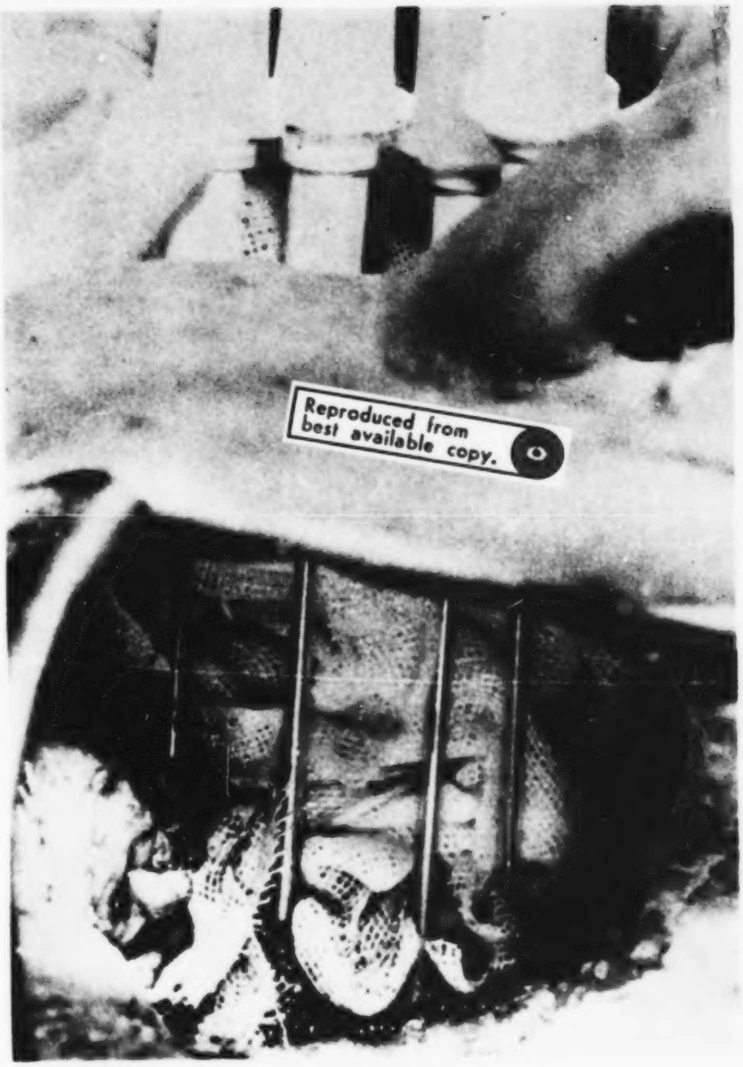

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Figure 7. Gauze packed to maintain position of angiocath tubes.

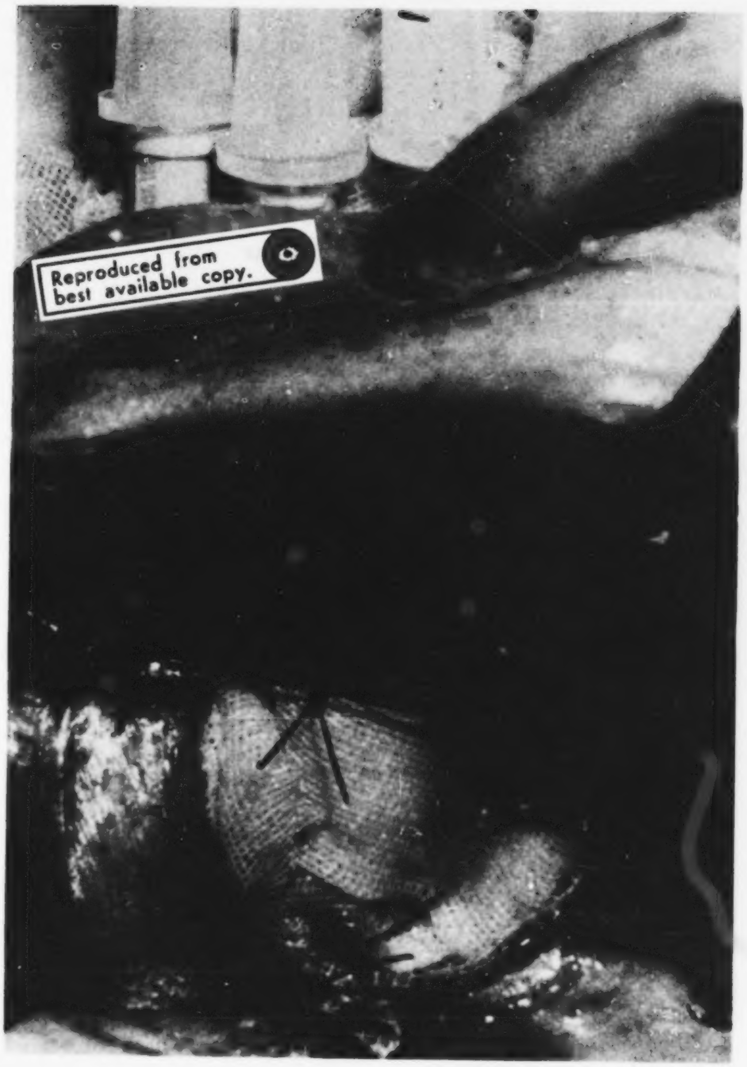

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Figure 8. Sutures retain packing.

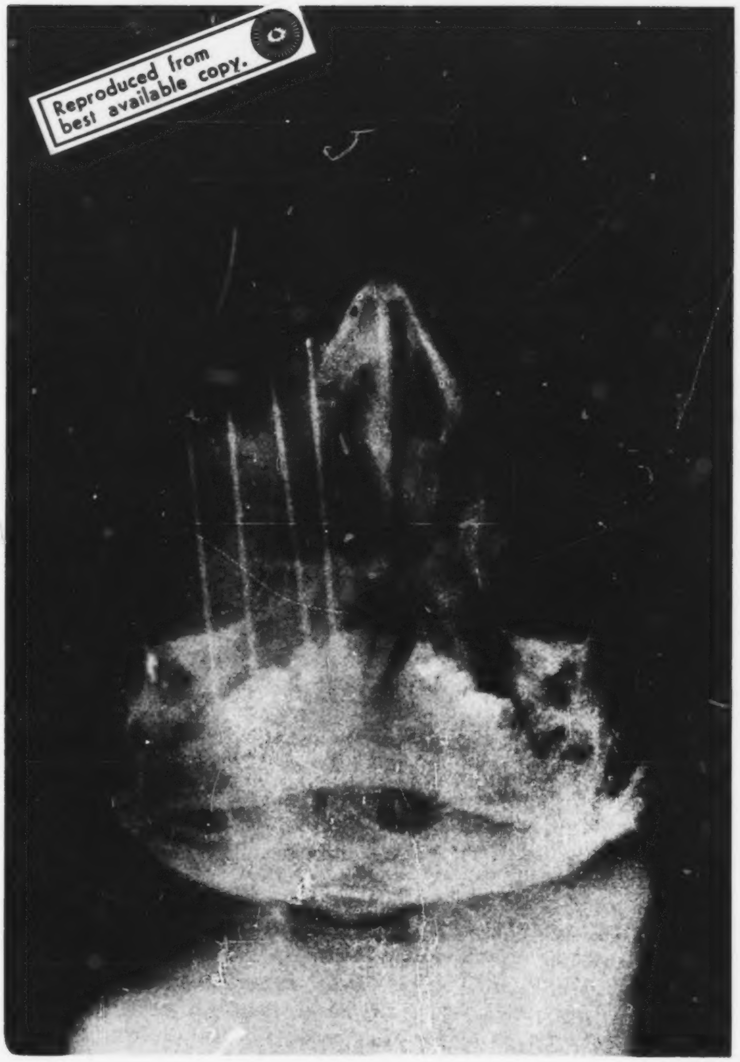
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Figure 9. X-ray film of array.

RADIOBIOLOGICAL CHARACTERISTICS OF CALIFORNIUM 252[1]

Harold L. Atkins, M.D.

Californium 252 now is in plentiful supply, due to production programs of the U. S. Atomic Energy Commission. This nuclide undergoes alpha decay and spontaneous fission, releasing radioneutrons and gamma rays with an effective half-life of approximately 2.6 years. Since only microgram quantities are required to produce dose rates adequate for interstitial radiotherapy, interest has been widespread in this potential application for californium 252.

A clear understanding of the radiobiological differences between gamma and neutron irradiation is necessary before applying californium 252 to problems of human malignancy. Three areas are worthy of consideration: (a) oxygen enhancement ratio values for continuous irradiation with neutrons and gamma rays; (b) health physics aspects of small doses of neutrons; and (c) RBE values for continuous irradiation.

OXYGEN ENHANCEMENT RATIO

The reduced oxygen enhancement ratio (OER) of neutron irradiation is the basis for using californium 252 in the treatment of malignant growths. In single acute exposures of neutrons of various energies, the OER usually has been about 1.5-1.6 (1). This would give a gain of $\sim$ 1.8, compared to x rays. For fission spectrum neutrons, an RBE of 1.2 has been observed (2).

Determining the OER with protracted continuous irradiation is extremely difficult. Maintaining the system being studied under anoxia for many hours, and even days, introduces a number of complicating factors. Nevertheless, we were able to determine the OER for HeLa cells in culture as 1.3 (3), compared to an OER of 2.9 for 250 KVp x rays (figure 1). Our studies are continuing with Chinese hamster lung cells. We have determined an OER of 2.6 for cesium 137 irradiation of hamster cells. This is of interest because Hall et al (4, 5) determined that protracted irradiation with gamma sources yielded reduced OER's (1.4-1.5) in cell cultures.

---

[1] Research supported by the U.S. Atomic Energy Commission.

It has been hypothesized that with protracted irradiation the only cell injury manifest is of the high LET type. Call survival curves show a reduced shoulder, consistent with the results of the lower OER (5). With protracted, continuous neutron irradiation, this effect would be expected to be even greater. It must be stated, however, that some studies have shown a somewhat higher OER with californium, in the range of 1.6-1.7 (6, 7).

RADIOBIOLOGICAL EFFECTS OF SMALL DOSES OF NEUTRONS

It is well recognized that the RBE for low dose effects of neutrons may be considerably higher than for high dose effects. This is a consequence of difference in the shape of cell survival curves. The lack of a shoulder in survival curves, due to cumulative effects of high LET radiations, and the presence of a shoulder in the curve for irradiation, due to the requirement of at least two events in the target volume for cell death, accounts for a gradually increasing RBE for neutrons as one looks for low dose effects. This is very well illustrated by Barenden (8), who showed the following RBEs at different levels of effect for fission spectrum neutrons on human kidney cells in culture:

Percent survival	RBE
80	6.1
20	3.4
5	2.6
1	2.3

A number of biological endpoints in mammalian systems have been studied with neutrons, resulting in a wide range of RBEs, from close to 100 for induction of lens opacities to about 1.0 or less for lethality (9, 10). Of particular pertinence to protection problems are the high RBE values for induction of cancer (11) and genetic damage (12). Rossi (13) has analyzed this effect from the standpoint of the microdosimetry. Since a single event from neutron irradiation is sufficient to inactivate a cell, the effect is linear relative to dose. With low LET the effect is nonlinear, since two or more events within a cell usually are required for cell death. This is less likely to occur at low doses (and at low dose rates). The relationship of RBE to neutron dose for lens opacities and cancer induction is shown in figure 2.

These facts are of importance from a protection standpoint. Of course, it does not mean that low dose effects are greater with neutrons, but that the x and gamma effects are relatively less. However, the important aspect is that neutron effects do not diminish as rapidly with lowering the dose rate, and the effects are cumulative with little recovery after each radiation damaging event.

RADIOBIOLOGICAL EFFECTS OF CALIFORNIUM 252

Insufficient background knowledge about neutron effects resulted in serious tissue damage to patients involved in the first clinical trial of neutrons in radiation therapy (14). A current effort to evaluate the efficacy of fast neutrons at Hammersmith Hospital, London, (15) is based on more precise preclinical experimentation. The major factor for concern is the time-dose relationship. Because of relative lack of recovery between fractionated doses of fast neutrons, the RBE increases with increasing fractionation (16).

No previous clinical experience with protracted continuous neutron irradiation has been available. We have studied this aspect of californium 252 irradiation both in tissue culture and vivo effects on skin reactions in pigs.

Initial studies on HeLa S3 cells in culture established that, at the dose rate used, the entire biological effect was due to the fission spectrum neutrons from californium. Irradiation was carried out at several dose rates, and compared to an acute irradiation experiment carried out with reactor-produced fission spectrum neutrons. When corrections were made for multiplicity because of the short generation time in cell cultures, no dose rate effect could be demonstrated (figure 3), quite different than for gamma irradiation (17). More recently, this was confirmed by Hall (18).

We are still in the process of studying the effects on pig skin of radium 226 and cesium 137 gamma radiation and the mixed gamma-neutron spectrum of californium 252. These studies confirm the cell culture data, and provide insight into the results obtained by the Hammersmith group, particularly evidence of rising RBE with reduction in the size of each fractional dose.

Fields of 36 cm^2 area have been irradiated on either side of the dorsum of pigs with gamma dose rates of 35, 67.8, and 192 rad/hour. Similar fields have been irradiated with californium 252 at dose rates of about 12.5, 15.0, 23.0 and 56.0 rads/hour. An additional set of fields now is under observation after irradiation at about 37 rads/hour. Reactions were scored on a 0-5 basis, level 5 being the fields demonstrating a moist reaction over more than 50 percent of the irradiated area. The results are shown in figure 4. Also shown is the result obtained by Archambeau (19) at this laboratory for an acute 250 KVp irradiation, corrected for RBE to give an equivalent gamma dose. This is plotted at 8.4 hours or 0.35 days, as suggested by Strandqvist (20).

The slope of the line showing gamma dose to achieve a radiation level of 5, versus duration of irradiation, is 0.29. This almost exactly parallels other data for human skin. On the other hand, the slope of the line describing the relationship for californium 252 is nearly zero. There is a dip near the very short exposure region, probably because of the increasing effectiveness of the gamma component at high dose rates. The result, then, is a variable RBE, depending on dose rate, as shown in figure 5. This is due to changing effectiveness of the gamma emitter with change in dose rate, whereas the total dose for californium 252 is relatively independent of dose rate.

It should be noted that these RBEs are for the total n + γ gamma emission of californium 252. Since the gamma component is effective particularly at the dose rates used clinically, it is reasonable to look at the neutron RBE. The n/γ ratio for these studies was relatively constant at about 60/40. This means the neutron RBE ranged from 5.5 to 7.5. That is equivalent to the very small fractions of neutrons in the analysis by Field (16) of RBEs from the Hammersmith data. This high RBE should be used in clinical situations, not the rather commonly stated RBE of 2.5-3.0 for acute single exposures of neutrons.

Studies also have been performed to determine the RBE for intestinal tolerance (21). As can be well imagined, it is difficult to determine RBE in experimental animals for protracted irradiation. The few clinical studies so far show results compatible with the animal studies (22).

CONCLUSION

The use of californium 252 for interstitial and intracavitary irradiation must be cautiously undertaken. The relative biological effectiveness of protracted neutron irradiation is much higher than might be supposed. This is important not only from a tissue tolerance standpoint during therapy, but also from the health physics standpoint for those occupationally exposed to the californium 252 sources.

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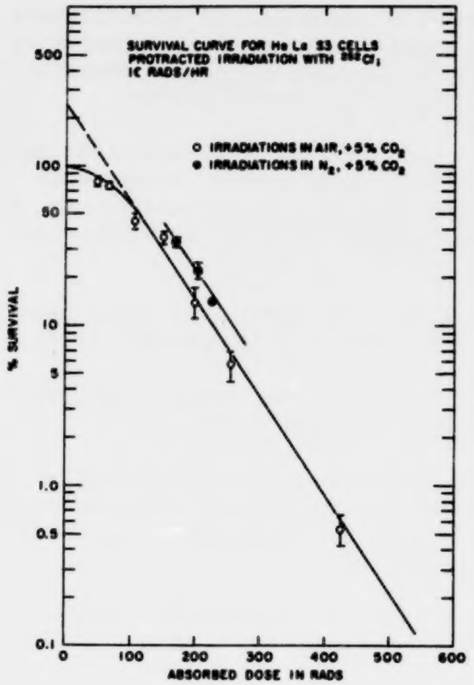

Figure 1. Response of HeLa cells to californium 252 in air and nitrogen (Fairchild, et al[3]).

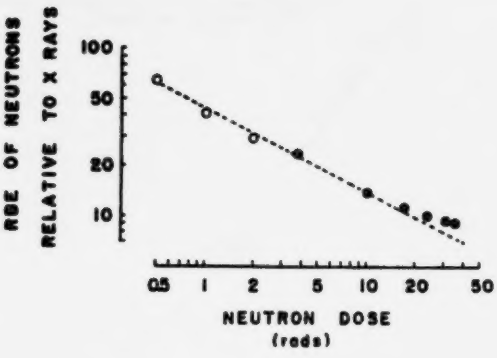

Figure 2. Relationship of RBE to neutron dose from Rossi (13). The open circles refer to murine cataract induction, the solid circles to cancer induction in rats.

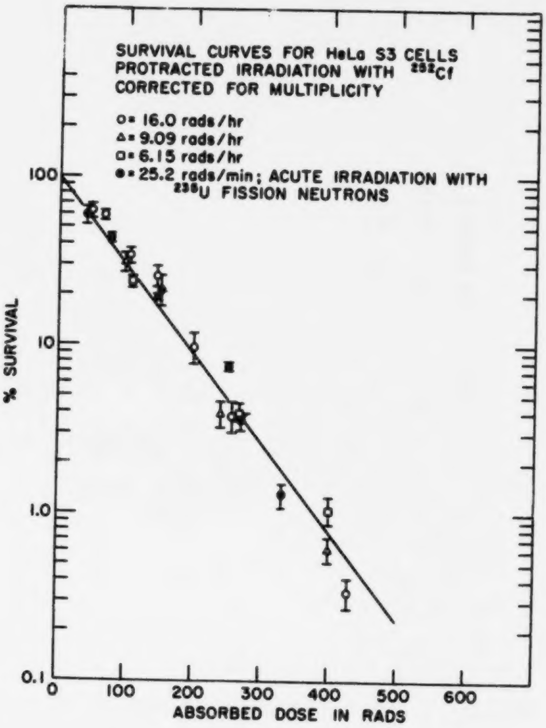

Figure 3. Effect of fission spectrum neutrons at different dose rates on HeLa cells in culture (Fairchild, et al).[17]

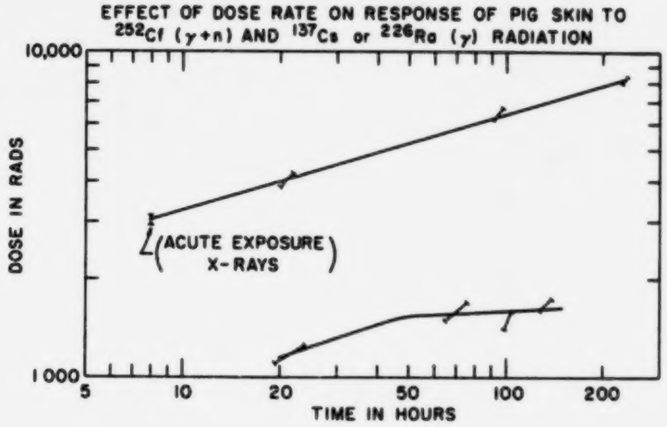

Figure 4. Skin tolerance levels in pigs following irradiation with gamma sources and californium 252 at various dose rates. Upper curve is gamma radiation, lower curve californium 252 irradiation.

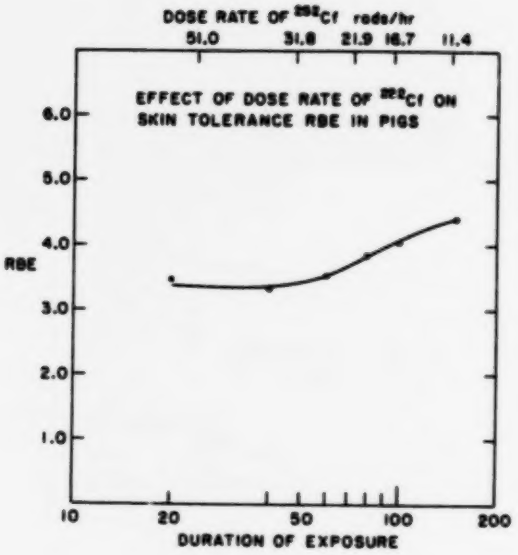

Figure 5. Variation of RBE with dose rate for californium 252 on pig skin.

AFTERLOADING OF CALIFORNIUM 252

George D. Oliver, Jr., Ph.D., and Joseph R. Castro, M.D.

ABSTRACT

The hazard to hospital personnel from californium 252 radiation, for quantities needed to give radiotherapy schemes equivalent to that of radium, is increased 5 to 10 times and possibly as much as 30 to 50 times. Reduction of dose to radiotherapy and nursing staff thus is essential to safe use of californium in clinical applications. Afterloading of sources should be considered a necessity, and bedside shielding should be utilized during treatment.

All types of interstitial and gynecological applications with californium can utilize afterloading with the proper technique and devices. Using these principles, procedures have been completed on 18 patients, resulting in an estimated maximum dose to the therapist of 1.2 mrem per implanted microgram of californium.

INTRODUCTION

Encouragement for the use of afterloading techniques in radiotherapy for neoplasms has derived from such credible reasons as improved treatment through accurate source placement and radiographic verification, and improved patient care, convenience, and safety. With the addition of californium 252 radiation as a potential clinical tool, another factor can be added to the list: that of necessity.

Californium 252 emits an abundant flux of fission neutrons with an attendant gamma ray field. The biological qualities of this mixed radiation field at low doses with low dose rates have been described by Dr. H. L. Atkins in the previous paper. The relative biological effectiveness is high and the oxygen enhancement ratio is low, creating a more potent radiation than conventional therapeutic radiation.

The dose for manifestation of radiation-induced cataractogenesis is known to be more than 10 times less for neutron irradiation than for gamma ray irradiation. At low doses delivered at low dose rates, an increased hazard of possibly 70 times may exist (1). For the incidence of genetic effects, in particular chromosome aberration, the hazard from neutrons is at least 5 times greater (2). For incidence of carcinogenesis, the hazard of neutron irradiation is 10 times higher, and (depending on the dose) may be as much as 30 times higher than for photons (3, 4). Based on the NCRP recommendations for personnel hazard evaluation, the mean quality factor (QF) for californium-type neutron fields should be 10, while the QF for radium should be 1.

With the increased hazard of californium use, caution must be exercised through detailed planning of the implant, adept loading and unloading, and use of special equipment during application. We have given considerable thought to simplifying and improving afterloading procedures at M. D. Anderson Hospital.

SOURCE DESCRIPTION

To understand our approach to afterloading californium, a knowledge of source types is needed. A radiotherapy source of californium 252 is constructed by uniformly electrodepositing californium hydroxide on a 90 percent platinum - 10 percent iridium wire. The deposition is flamed to californium oxide to increase the adherence of the deposit.

The prepared source is doubly encapsulated in a platinum - iridium cell and sheath (5). The assembly shown at the left of figure 1 is an afterloading cell with an outer diameter of 0.95 mm and an active length of 15 or 30 mm. Intensities for interstitial work have been 0.5 microgram/cm (full intensity) and 0.3 microgram/cm (half intensity).

The applicator tube on the right is fabricated similarly, and has the dimensions of a 15 mg radium tube: outer diameter is 2.8 mm and the active length is 15 mm. Tube activities range from 5 to 20 micrograms each.

Methods and materials required for implanting depend on the source dimensions. The 0.95-mm diameter has been considered too large for an afterloading system that is simple yet efficiently loaded. Collaboration of therapists and source fabricators has resulted in Savannah River Laboratory researching the concept of:

1. A californium wire (O.D. $<$ 0.5 mm);
2. A californium call singly encapsulated in a stronger material than platinum-iridium, such as stainless steel (O.D.$\sim$ 0.6 mm).

INTERSTITIAL AFTERLOADING

Techniques of californium source placement in localized superficial and intraoral tumors have been modifications of those suggested by Pierquin (6) and Henschke (7). To illustrate, an example patient has been selected.

The patient (figure 2) had a squamous cell carcinoma in the right neck, metastatic from the lungs. The therapist planned the double plane implant (figure 3).

The first step is percutaneous insertion of unloaded Teflon tubes into the tumorous region through use of a stainless steel spear with a trocar point (figure 4). The outer diameter of the spear head and tubing are the same, in order to present a smooth surface, and the tubing slips easily down the shaft to fit snugly on a shoulder of the spear head. A pin vise is clamped at a convenient position to facilitate handling during insertion. The diameter (2.0 mm) is considered too large and potentially traumatic to the patient. Either of the two sources under investigation would reduce the diameter to about 1.6 mm, the diameter of radium needles. Once appropriate positioning in the tumor is accomplished, the spear is removed, leaving the hollow tubing in place (figure 5). Special buttons are fitted on each tube end. Dummy sources with the same dimensions as californium cells are enclosed in nylon tubing according to implant prescription as far as strength, length, and number (figure 6). The button shafts are crimped, completing the procedure.

A modification of this technique is necessary for intraoral implants. The rigid spear shaft is replaced by a flexible steel cable (figure 7). The spear head is detachable and has several straight or curved substitutes. The flexibility allows for a second pass through the tumor from inside the mouth, forming a continuous loop accessible from both ends under the chin. In the case of tumors accessible only from one side, such as urethral or vaginal tumors, another modification uses hollow stainless steel needles as a substitute for the tubing. Each button is welded to the shaft, to allow for suturing in place.

To complete the example patient, a set of AP and lateral or stereoscopic radiographs are taken for source localization and anatomical verification, and to define the implant geometry for dosimetry calculations with a computer (figure 8). Earlier in this conference, Stovall and Shalek described the techniques and data for obtaining dose calculations in selected planes through an implant. The arrows in the figure mark the plane of calculation, which bisects the implant and lies perpendicular to the source direction.

A program (CALRAD) calculates the neutron and gamma ray dose components (8). Figure 9 presents the neutron isodose contour plot on the left and the gamma ray on the right for the mid-source plane. Source projections above the plane are represented by the solid line, below the plane by the dotted line. Anatomical points, such as an eye lens, can be coded for location and dose numbers. The treatment dose rates selected were 7 rad/hr neutron and 4 rad/hr is obtained by weighting each dose component by an appropriate clinical RBE and adding these; i.e., 7.5 (neutron dose rate) + 1.0 (gamma ray dose rate). The selection of an RBE of 7.5 is conservative, and has been examined (8).

The source loading takes place in the patient's room, after surgical recovery and radiographs. The dummy sources are replaced by californium sources, arranged in the identical manner. During all source procedures a bedside shield is interposed between the patient and the therapist (figure 10).

In most instances loading proceeded rapidly, but some were difficult due to curvature of the tubing in the implant, and inflexibility of the sources. The loop technique is particularly difficult for the source lengths we have used. It is possible to get afterloading cells of 0.5 cm active length, and use them around the curvatures. This type source would permit proper end crossing of the implants.

INTRACAVITARY AFTERLOADING

In the instance of treatment of carcinoma of the cervix, the afterloading applicators already used with radium can be utilized. The californium afterloading tube is the same size as a 15 mg radium tube and will maintain the dimensions for any activity of loading up to 20 micrograms. For gynecological use, we have calculated that the californium activity in micrograms should be about 40 percent of radium activity, in mg, to give approximately 40 rem/hr. (This value assumes the neutron RBE to be 7.5.) For example, the one gynecological case we have encountered was a six-source Suit-Fletcher afterloading tandem. The total activity was 40.5 micrograms (6.5 + 6.1 + 6.0 + 5.4 + 8.0 + 8.6). The two exterior sources were surrounded by 3.0 cm vaginal cylinders of lucite. When ovoids accompany the tandem, Fletcher-Suit afterloading colpostats are suitable.

Although the dose to the attending physicians with applicator afterloading is nominal, the dose to the nursing staff is not. One way to alleviate their dose is to use a remote afterloading device, such as that designed and built by E. B. Moore at M. D. Anderson Hospital (figure 11a). This device pneumatically delivers preloaded sources from a portable safe into a tandem and/or ovoids. A timer is provided to record actual treatment time. When the patient under treatment requires extended care, the nurse places the sources in the safe by remote control while the patient's applicators remain in treatment position. For californium use (figure 11b), additional neutron shielding can be added without loss of function. The white block of shielding for californium neturons is at least 4 HVT (9).

BEDSIDE SHIELDING

Additional shielding adjacent to the patient should be used for interstitial implants (figure 12). The therapist was shown loading an implant behind a one-man shield; another version exists for two-man operations. This double shield is left in place next to the patient's bed for the treatment term. The shield body protects the total body with 3 to 4 HVL, while the plastic face shield protects the eyes with a 2 HVL thickness.

PERSONNEL DOSES

Therapists have been monitored for neutron doses during all source-handling procedures. Since no adequate personnel dosimeters (including film badges) are commercially available, the dose was estimated with a tissue-responding monitor. A quality factor of 10 was used to convert from rads to rems. With the implant fully loaded, dose rate behind the face shield was measured. The therapist was timed during the loading and unloading procedures. Since the actual dose rate was increasing or decreasing, the measure employed is the maximum probable dose to the eye lens of the therapist.

Figure 13 presents this neutron dose normalized to the number of micrograms of californium 252 implanted for each of the 18 patients. No data were obtained for patient 2, due to loading in the operation room. Excluding patients 12 and 14, the dose/implanted microgram averages 1.2 mrem. The average implant is 17 micrograms; so the therapist received less than 20 mrem per case. Patients 12 and 14 had vaginal implants that required removal of the shield in order to unload the implant. Patient 18, who had the gynecological implant, had a low value because of speedy source handling for the large quantity of californium.

SUMMARY

It is evident that radiotherapy with californium 252 sources presents a greater hazard to hospital personnel than does radium. Hence, the use of afterloading techniques is necessary. Correspondingly, bedside shielding and modifications of conventional approaches help reduce the hazard to a level that allows the use of these sources.

Afterloading implants provide the opportunity for better patient treatment by removing the pressure of extensive work in a radiation field, by enabling better planning of the implant, more accuracy of source placement and verification for suitable coverage of the tumor. Knowledge of the dose configurations before treatment enables adjustment of anticipated loading distribution and source intensity, for optimal treatment.

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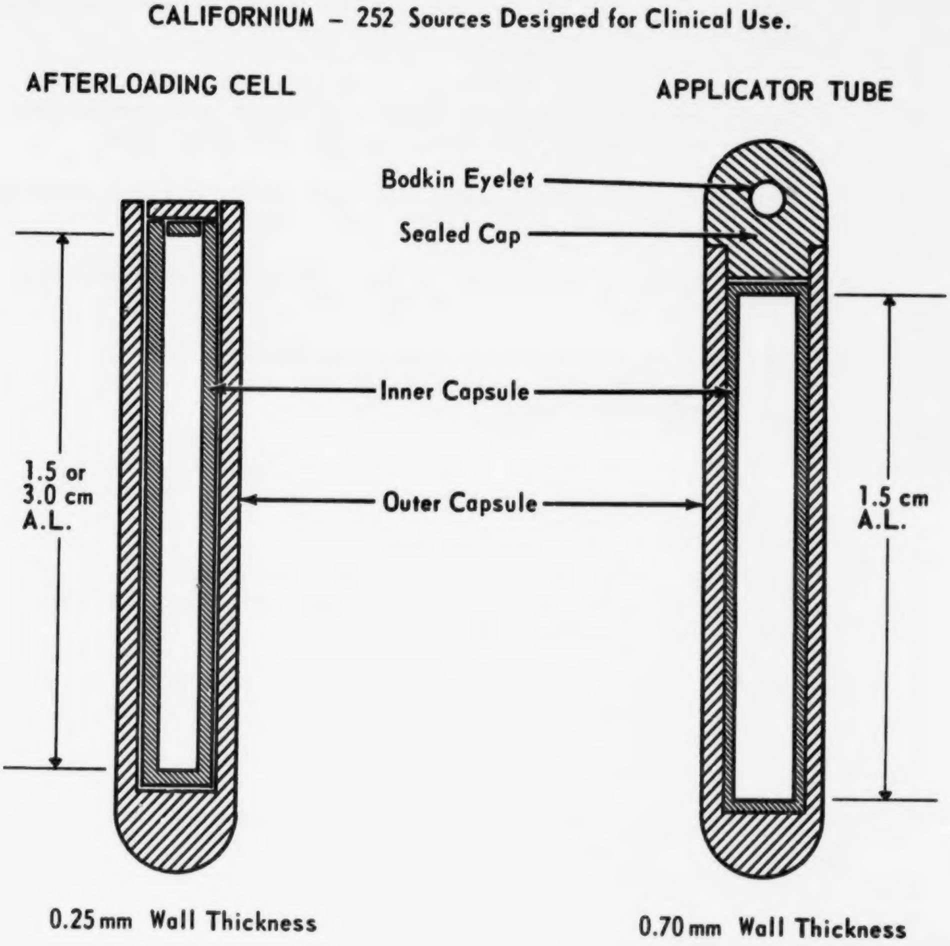
CALIFORNIUM – 252 Sources Designed for Clinical Use.
AFTERLOADING CELL
APPLICATOR TUBE
Bodkin Eyelet
Sealed Cap
Inner Capsule
Outer Capsule
1.5 or 3.0 cm A.L.
1.5 cm A.L.
0.25 mm Wall Thickness
0.70 mm Wall Thickness

Figure 1. Californium source types. The afterloading cell for interstitial implant is on the left, the afterloading tube for gynecological implants is on the right.

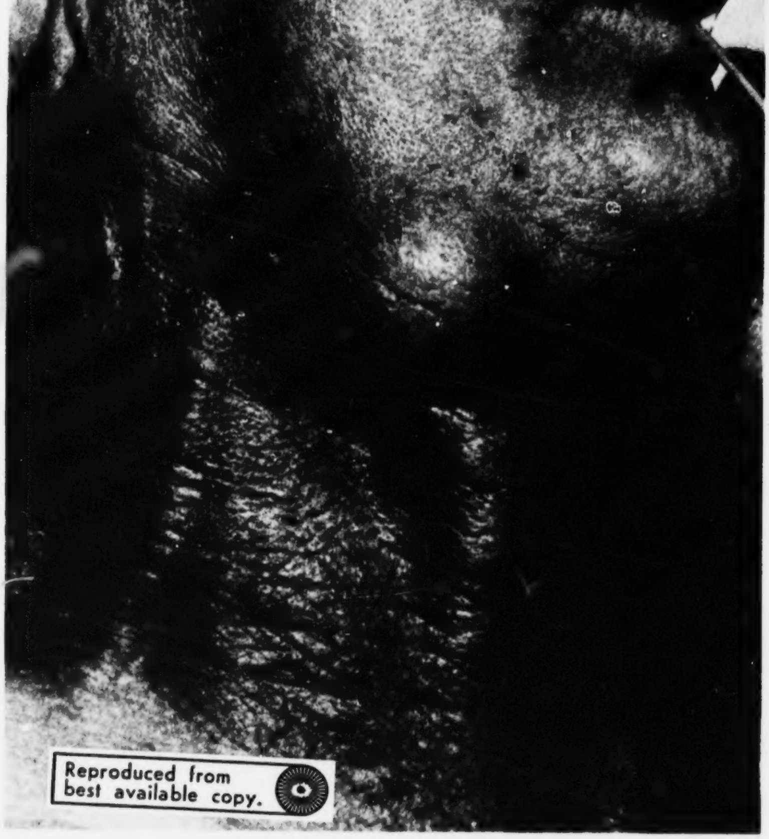

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Figure 2. Neck node of example patient

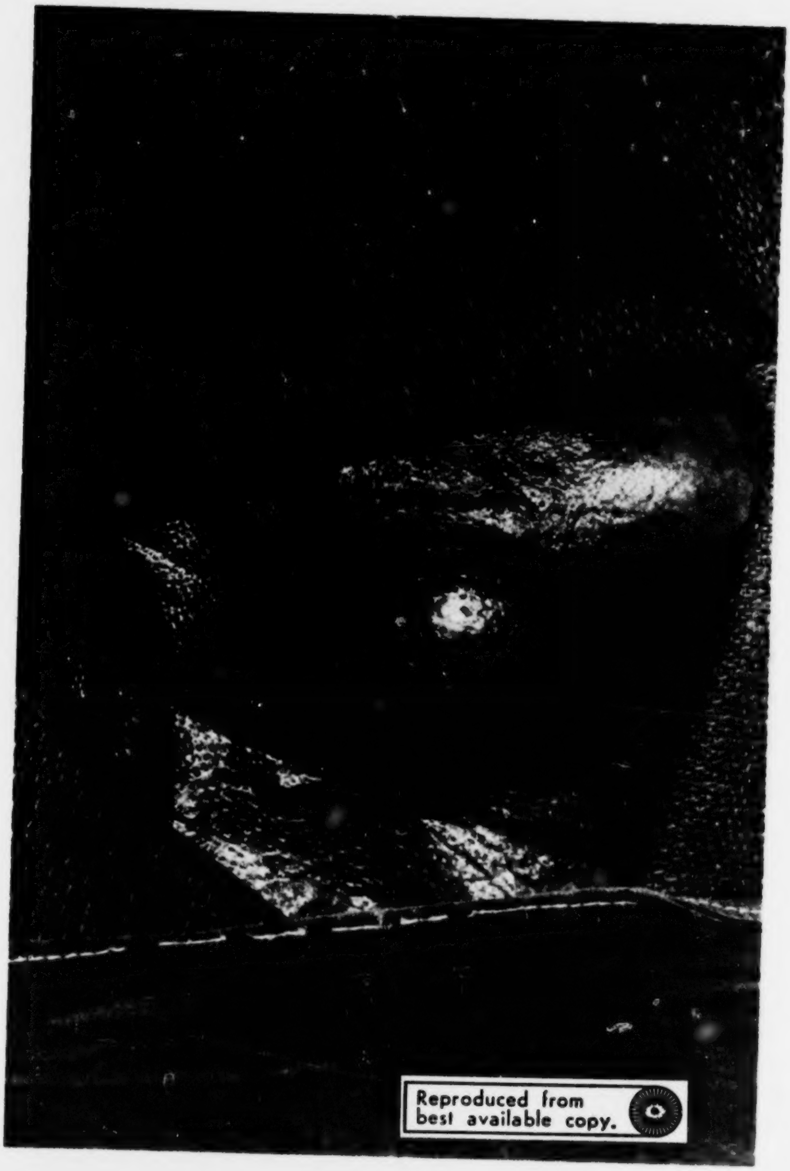

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Figure 3. Planning of implant in surgery

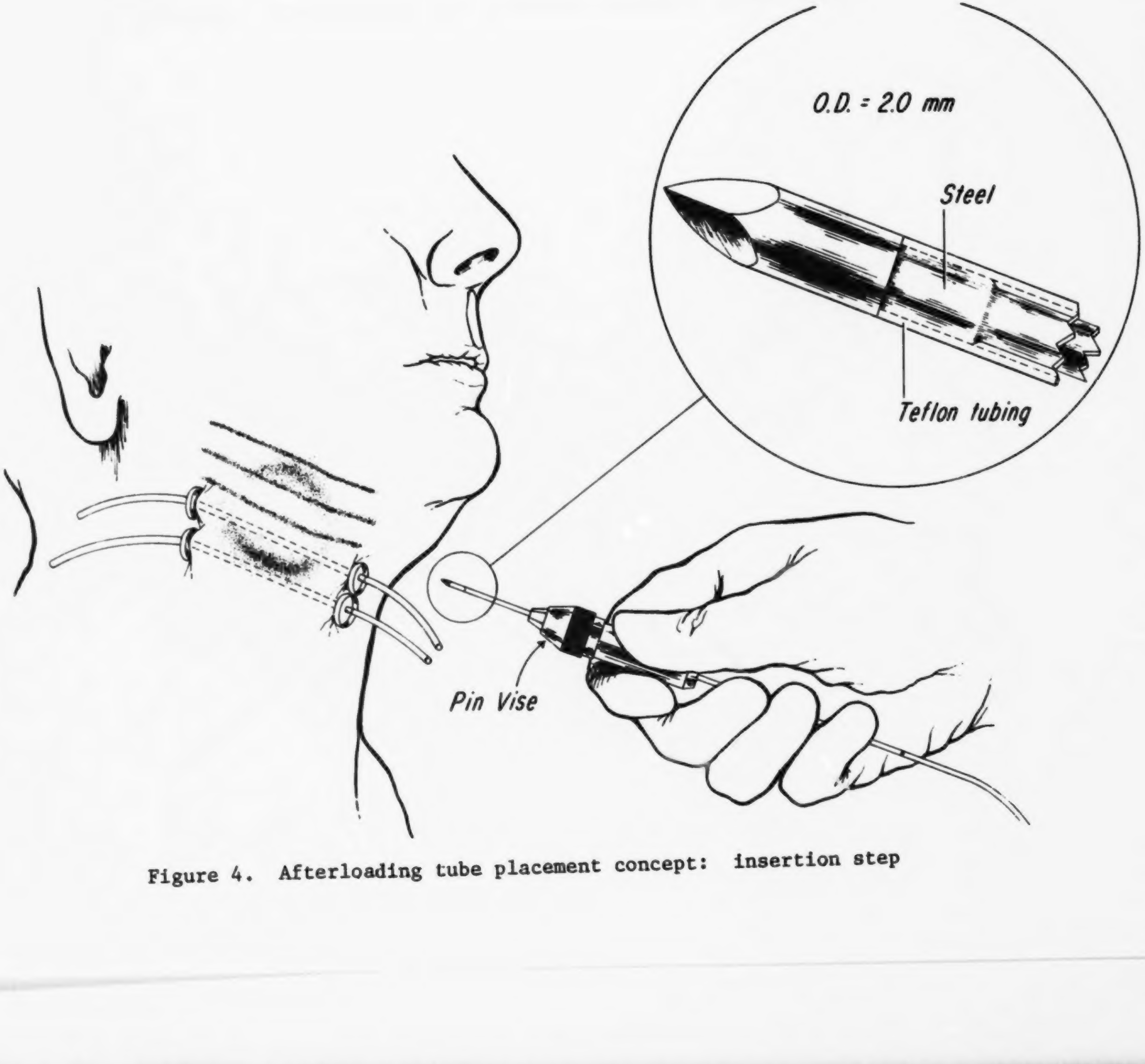
O.D. = 2.0 mm
Steel
Teflon tubing
Pin Vise

Figure 4. Afterloading tube placement concept: insertion step

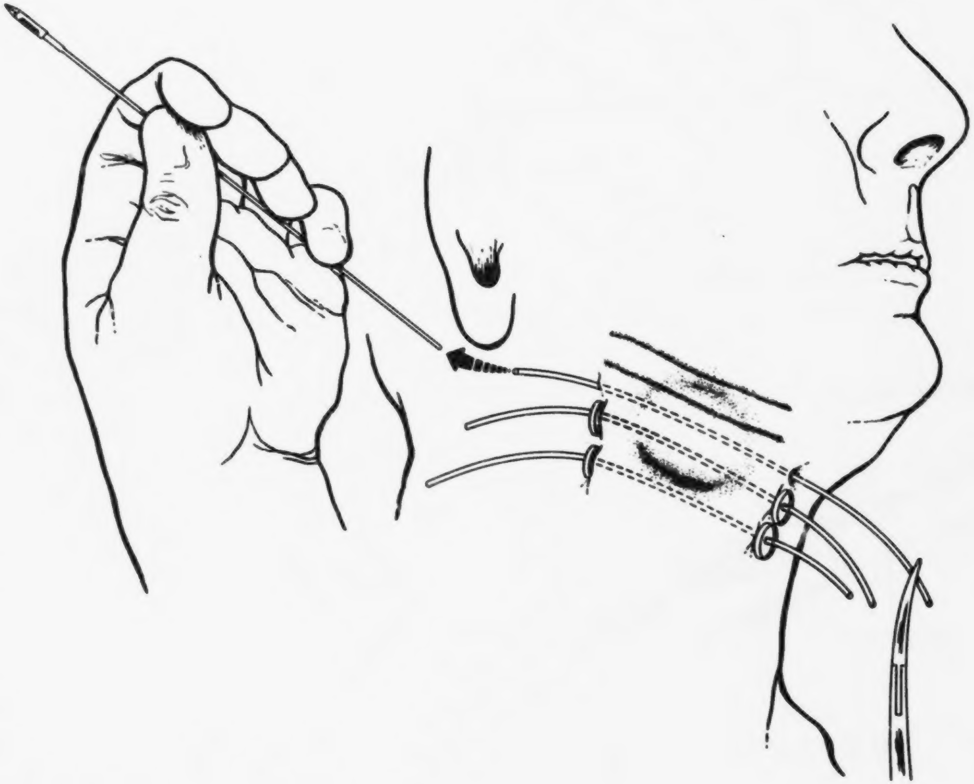

Figure 5. Afterloading tube placement concept: spear removal

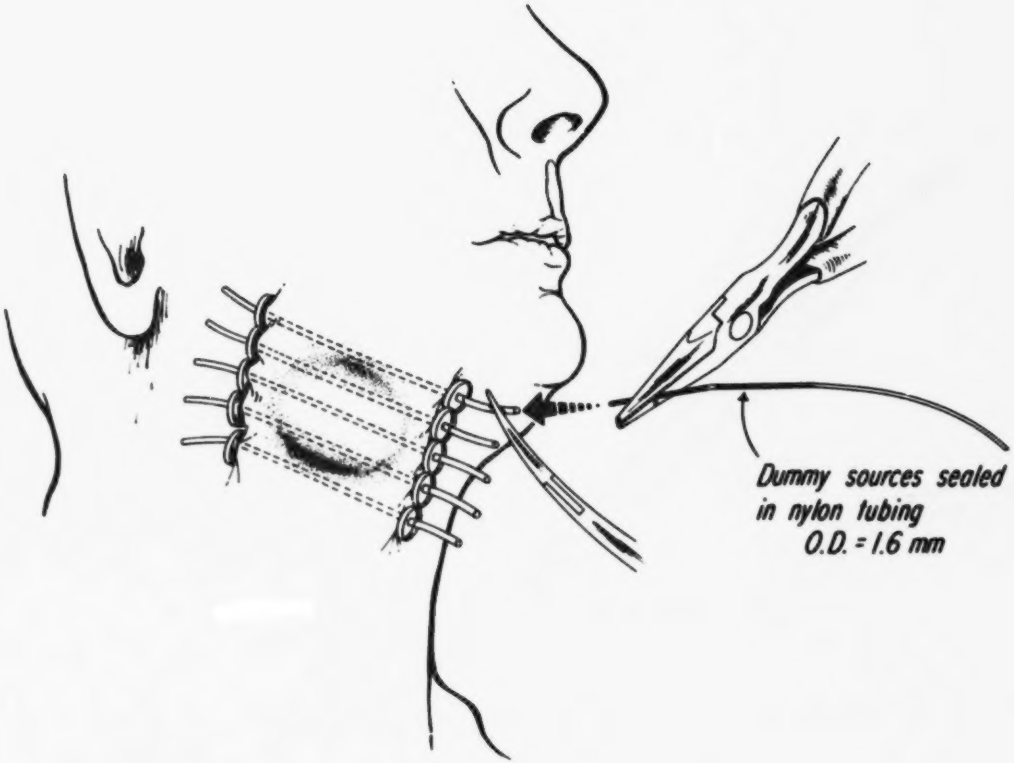
Dummy sources sealed
in nylon tubing
O.D. = 1.6 mm

Figure 6. Afterloading tube placement concept: source placement

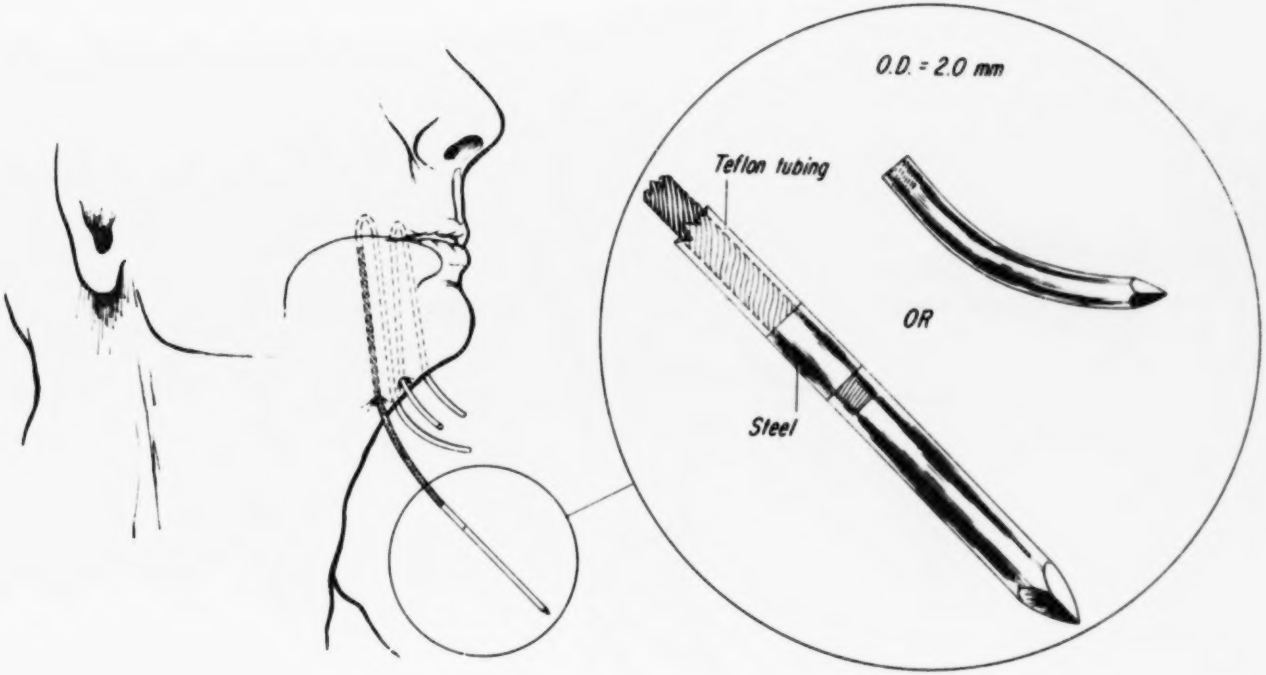
O.D. = 2.0 mm
Teflon tubing
OR
Steel

Figure 7. Afterloading concept: loop technique

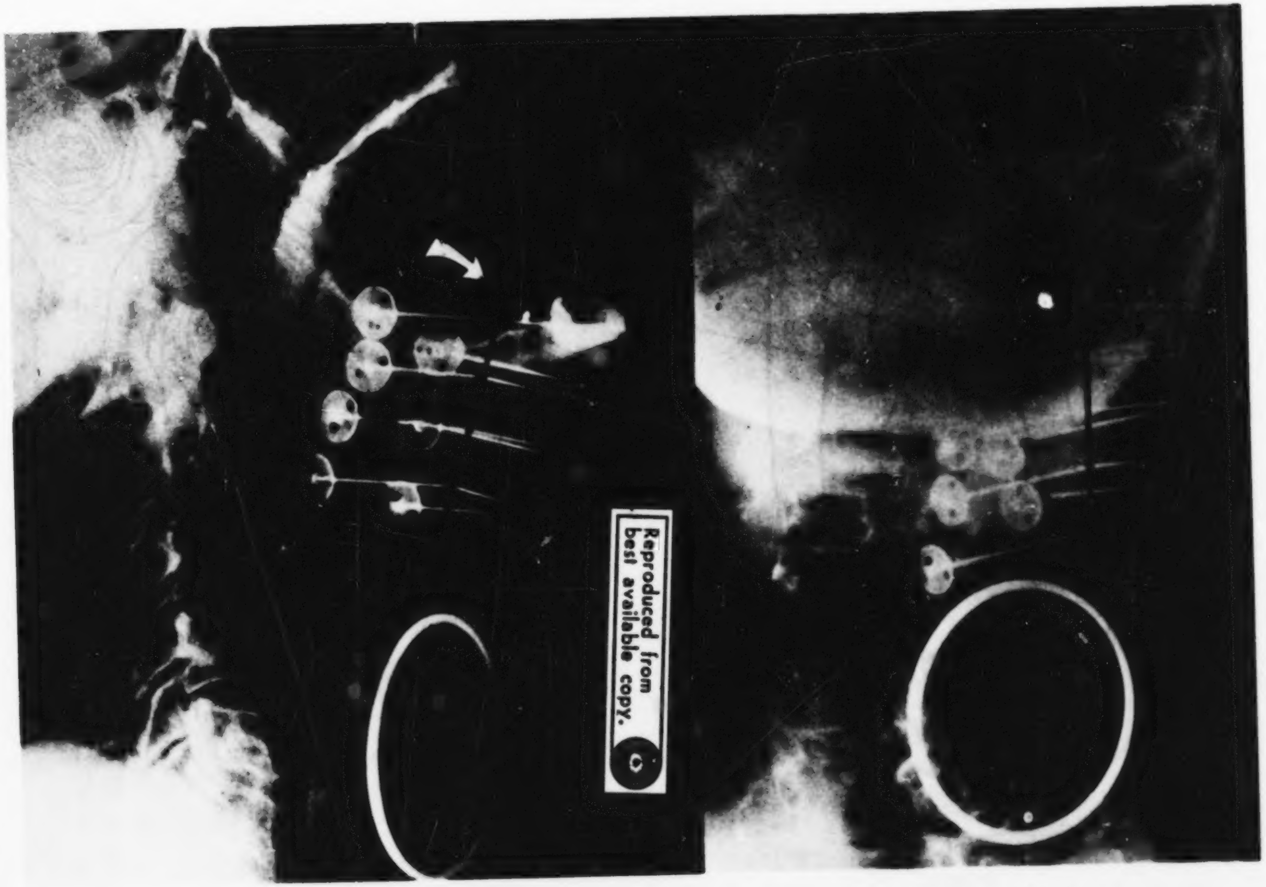

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Figure 8. Radiograph of AP, and lateral views of example patient with implant loaded with dummy sources

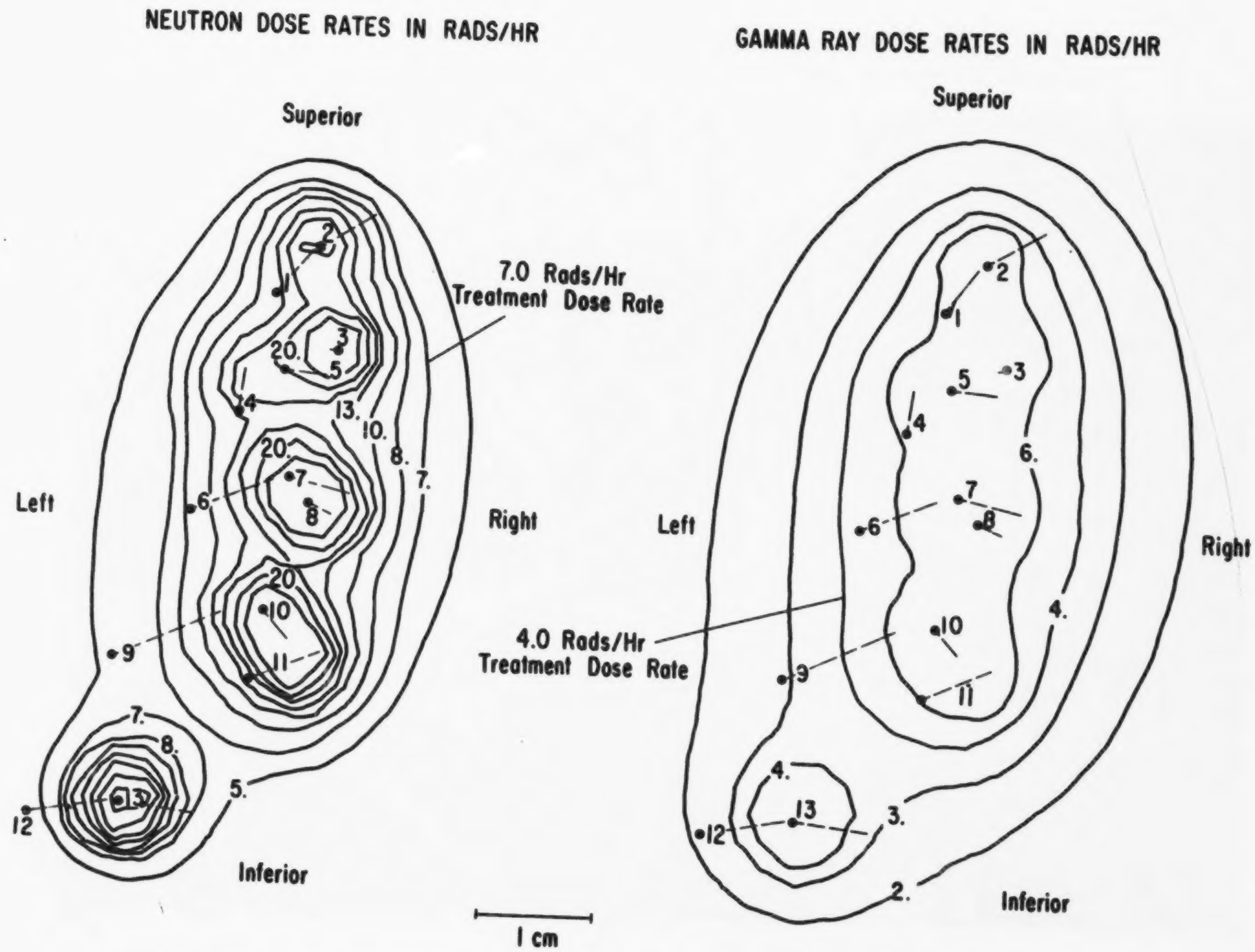

Figure 9. Calculation of neutron and gamma ray dose components in example patient

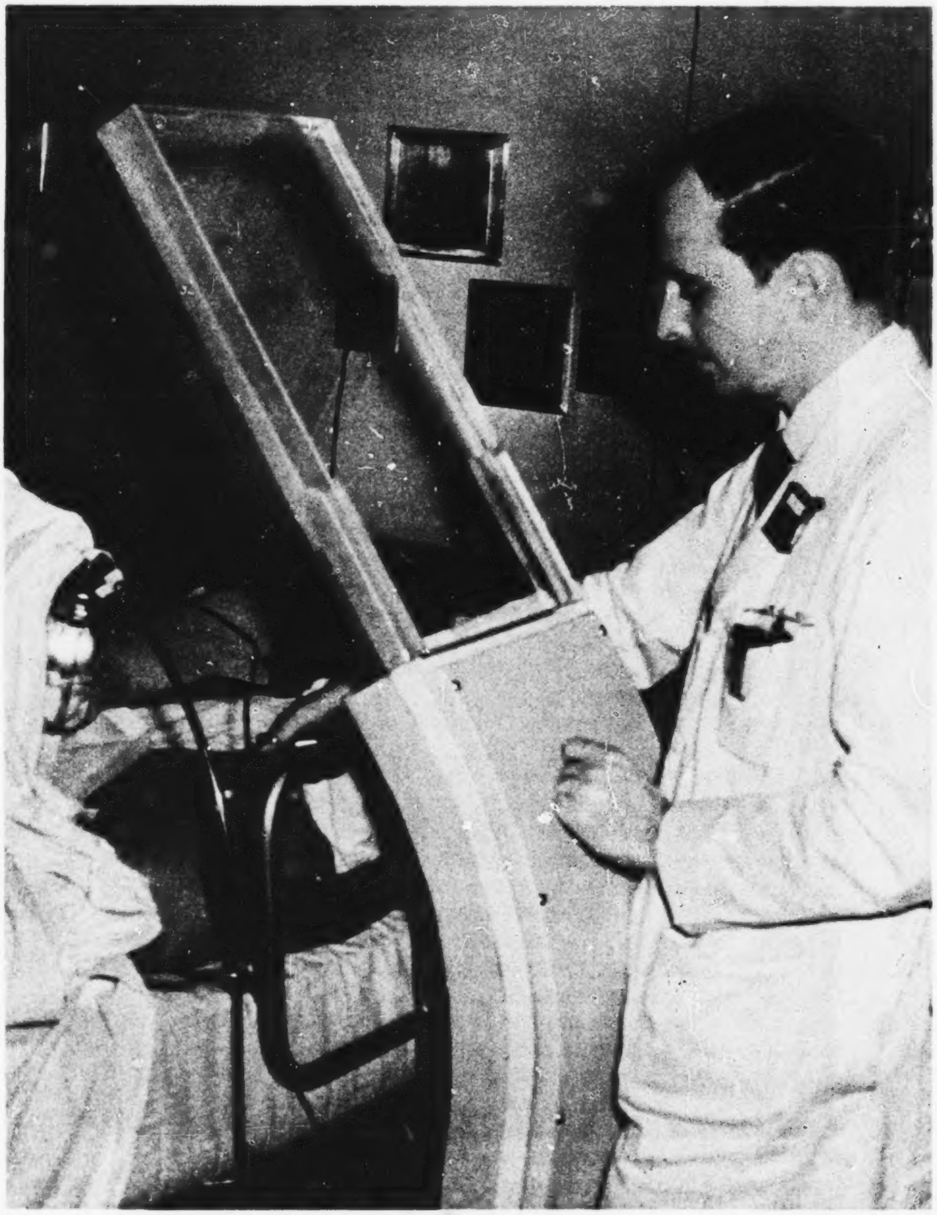

Figure 10. Afterloading procedure at patient's bedside, with shielding

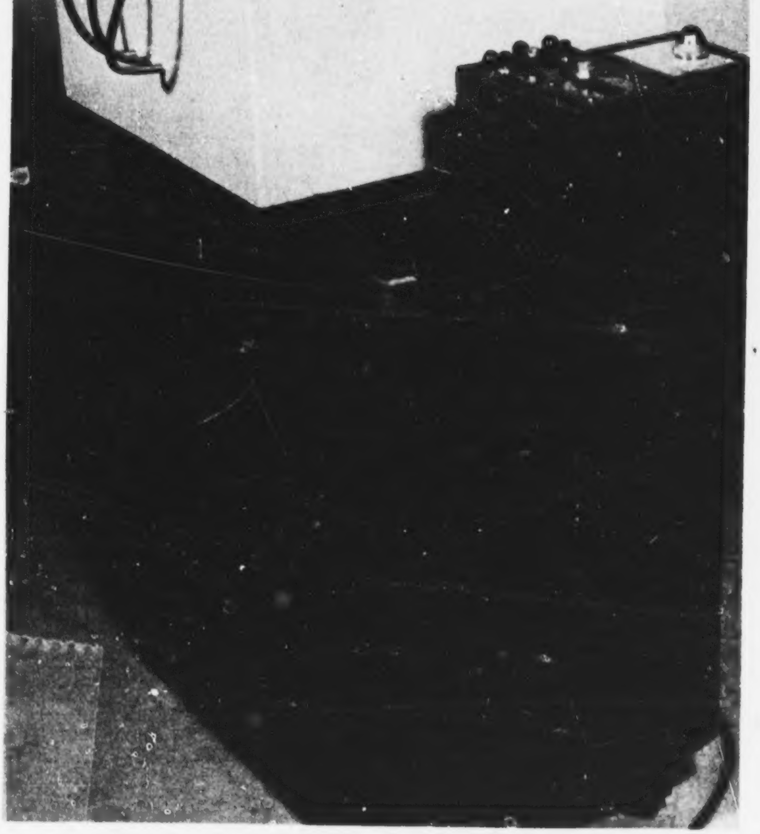
CAUTION
RADIOACTIVE MATERIAL

Figure 11a. Remote afterloading device for radium use

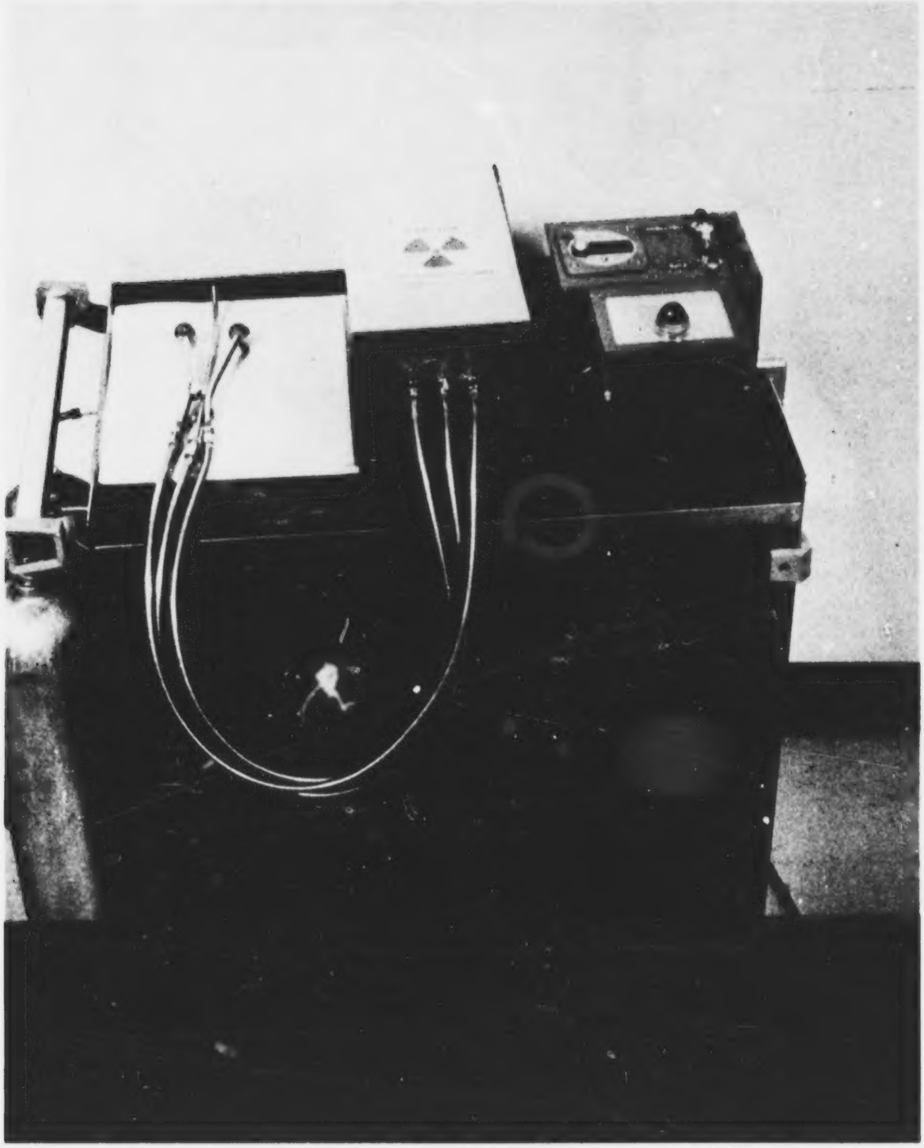

Figure 11b. Remote afterloading device, modified for californium use

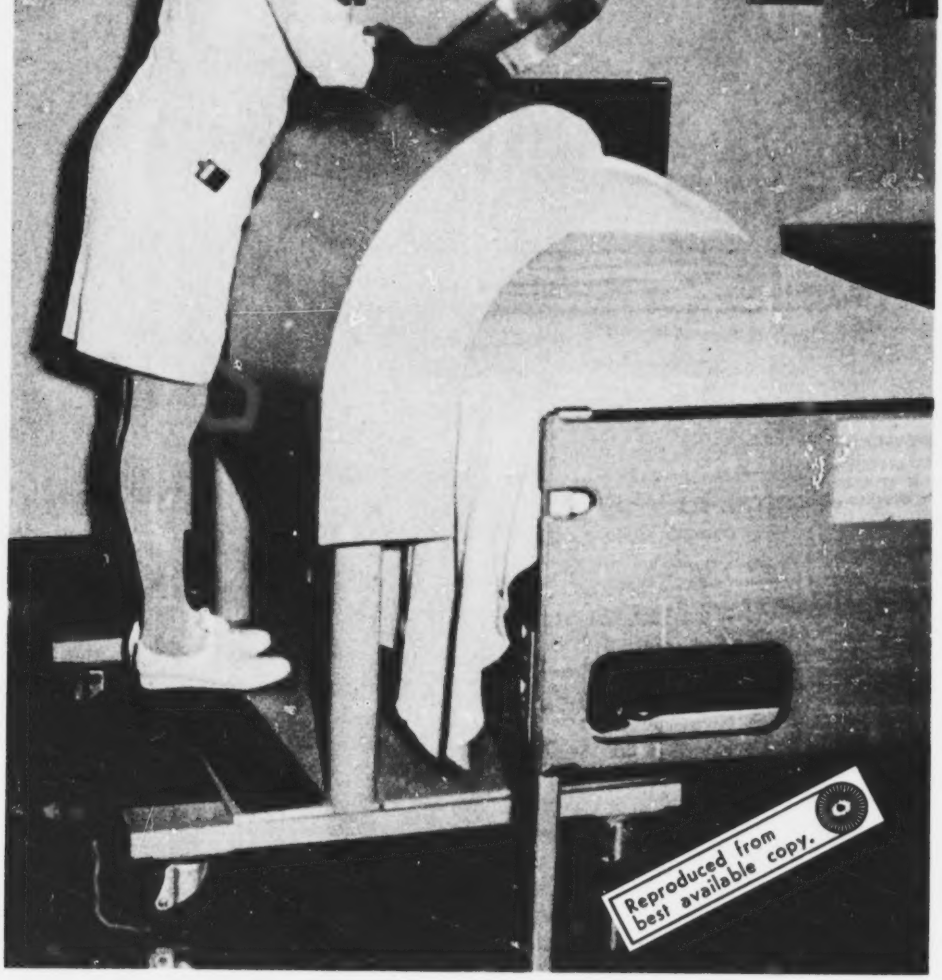

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Figure 12. Bedside shield for two-man procedures

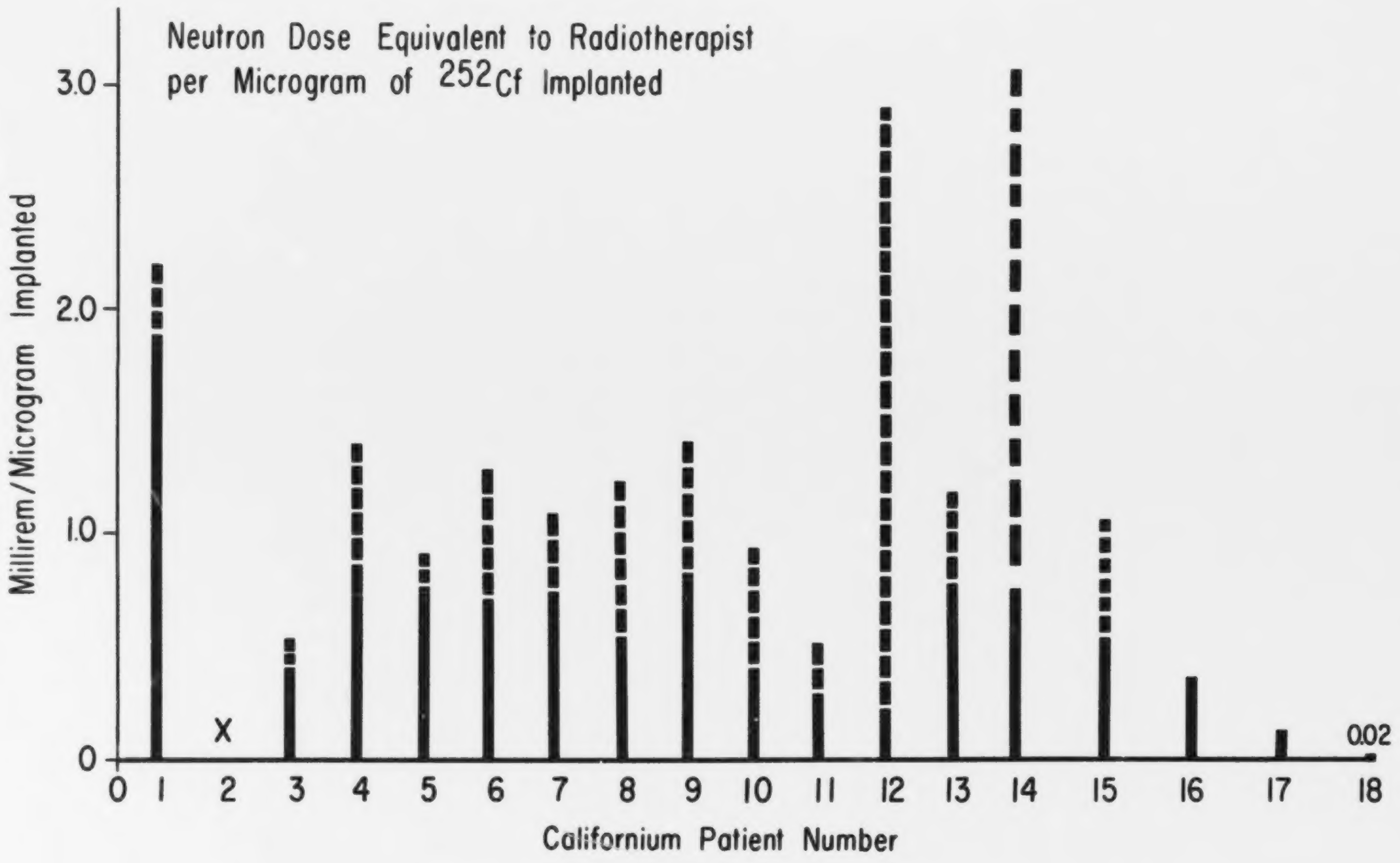

Figure 13. Measured exposure rates to the therapist, behind shielding per microgram of californium-252 afterloaded in the implant

DISCUSSION

CHAIRMAN J. BOLAND: May I start the questions by asking, since palliative treatment can be given by external sources without any radiation hazards, what is the justification for using a radioactive source to complete this treatment?

DR. HENSCHKE: We have always stressed that interstitial implantation should be used only if external radiation cannot deliver a sufficient dose. In general, we give external radiation therapy first; only when the dose the tumor requires cannot safely be delivered by external radiation do we use interstitial therapy. However, there are one or two exceptions.

If you have a patient coming from far away with a small skin nodule, and you don't want to put him through a long course of therapy and you are reluctant to give one or two doses with external radiation, then I think there is reason to put in a small permanent implant and let the patient go home. We have done this successfully, particularly in developing countries where there's a great shortage of beds and facilities.

But interstitial radiation generally is only supplementary to external radiation, to be used in a small number of patients, usually in a tumor that cannot be controlled by external therapy.

DR. HILARIS: At Memorial, if a small tumor recurs after irradiation therapy and there's no room for further external irradiation, we do an implant. Otherwise, I don't think there is any indication for palliative implants.

DR. CHARYULU (Miami): I'd like to add my own comments. I feel that cure rates with external therapy alone are not satisfactory unless doses of about 6,000 rads are given. This dose naturally has associated morbidity in the patient. I think we can minimize the morbidity, and at the same time achieve better cure rates, by elective implantation in association with external therapy. Of course, the time when you would combine external and internal therapy is up to the individual therapist. But I suppose it's a good idea to stop external therapy after about 1,000 to 1,500 rads, and then implant, giving a dose up to 7,000 or 8,000 rads by the combined approach.

STANDARDIZATION OF SOURCES

SEALED SOURCES OF RADIOACTIVE MATERIAL: PERFORMANCE STANDARDS AND REGULATORY CONTROL

James C. Malaro, Jr., B.E.

INTRODUCTION

The use of sealed radioactive sources in radiotherapy has grown significantly in the past 10 years. Those now available to the radiotherapist range from large teletherapy sources to radioactive needles and tubes used for implantation or in afterloading devices.

The Atomic Energy Commission (AEC) and certain state licensing authorities regulate the use of such sources by the radiotherapist. In carrying out this regulatory function, the AEC with the assistance of its medical advisory committee must consider a number of factors, including the qualifications of the physician, his equipment, facilities and procedures, the radioactive source he proposes to use, and the efficacy of the proposed method of treatment. This paper will deal only with evaluation of the ability of the source to maintain its integrity (i.e., contain the radioactive material) under expected conditions of use.

REGULATORY AUTHORITY

Under the Atomic Energy Act of 1954 as amended, the Atomic Energy Commission is authorized to regulate the use of most radioisotopes and other atomic energy materials to protect both the common defense and security and the health and safety of the public. The Act authorizes the AEC to license the use of byproduct, source, and special nuclear materials. Naturally occurring radioactive materials (e.g., radium 226) and radioactive materials produced in an accelerator (e.g., cobalt 57) are not directly subject to AEC licensing authority.

Under the provisions of a 1959 amendment to the Act, the AEC has entered into agreements whereby certain of its regulatory responsibility and authority have been transferred to individual state governments. At the present time there are 23 such Agreement states.

EVALUATION AND CONTROL

Prior to licensing a physician to use a sealed source for radiotherapy (afterloading, interstitial, intracavitary, teletherapy, etc.) the AEC (or state regulatory authority) requires a complete description of the design, manufacture, and testing of the source.

As a convenience to the distributor, user, and regulatory agency, distributors of sealed sources are encouraged to submit the required information so that the sources may be evaluated by the regulatory agency prior to receiving requests from radiotherapists to use these sources. This eliminates the unnecessary delays that may result when technical review of the source must be made concurrently with review of the radiotherapist's request.

When evaluating a sealed source for licensing purposes, the two major questions to consider are: (1) can the source be expected to maintain its integrity under expected conditions of handling, use, and possible abuse? and (2) what can be expected to happen if the source does lose its integrity? To be able to answer these questions, the reviewer requires among other things the following information either from the manufacturer, distributor, or user of the source:

1. Proposed use of the source and identification of the environments and operating conditions expected during normal use;
2. Identification of the radioactive material, maximum activity per source, chemical and physical form, and method of deposition of the radioactive material in the source capsule;
3. Drawings or sketches of the source capsule describing all materials of construction, dimension, and methods of sealing the source;
4. Description of tests performed on prototype sources that established the integrity of the source construction and seal under the most adverse conditions of use to which the source is likely to be subjected. (These prototype tests should reflect the actual conditions of use.); and
5. Description of the quality control procedures used to assure that each finished source will meet the specifications furnished to the AEC. The quality control program normally includes procedures for checking for source leakage and construction defects.

PERFORMANCE STANDARDS

To assure effective containment of the radioactive material in sealed sources, performance standards have been developed by a number of standards groups including the International Atomic Energy Agency (IAEA) and the American National Standards Institute (ANSI). Oak Ridge National Laboratories (ORNL) also has developed performance recommendations. These standards and recommendations are used by the AEC and other regulatory organizations in developing regulations and licensing criteria for the use of the sources.

In 1962 a group composed of manufacturers, representatives from national laboratories, and representatives of other interested groups formed the American Standards Association (now the American National Standards Institute) Committee N5.4 to consider standards for the safe use of sealed radioactive sources. Two representatives from the AEC served as liaison members on this committee. The work of the group culminated with the publication in April 1968 of the USA standard "Classification of Sealed Radioactive Sources," USASI N5.10-1968. This standard classifies sources according to their ability to withstand thermal and mechanical stress including pressure, impact, vibration and puncture. This classification system now is widely used by source manufacturers in the U. S. and the International Standards Organization (ISO) is considering adopting a modified version as an international standard.

The AEC has encouraged manufacturers and distributors of sealed sources to adopt standard methods for measuring source performance, since the use of such standards simplifies communication and can result in uniformly high source quality, without discouraging design innovations. In addition, it provides the AEC and other regulatory agencies with a common basis for evaluating new sources.

Some medical sources are exposed to abnormal environments, and the adequacy of their design for the intended use must be considered on an individual basis. Californium 252 medical sources currently available from the AEC Savannah River Operations Office, for example, are -- in addition to the usual thermal and mechanical tests -- tested for corrosion resistance and aging effects due to prolonged exposure to fast and thermal neutrons. To deal with specialized problems unique to medical uses, additional standards are being developed by standards groups, including ANSI and ENEA (European Nuclear Energy Agency). ANSI Subcommittee N44.2, for example, is developing a standard entitled "Integrity Standards and Test Specifications for Selected Brachytherapy Sources," and the ENEA is working on a standard specifically designed for nuclear-powered cardiac pacemakers.

The radiation safety experience with sealed radioactive sources used for radiotherapy in the U. S. has been quite encouraging. Of the thousands of sealed sources containing byproduct material used by the radiotherapist in the past 5 years, only 23 have been reported as suspected of leaking radioactive material. This is based on the presence of 0.005 microcurie or more of removable contamination on the source or source container. During this period, there has been no report of leakage serious enough to lead to significant exposure of personnel or contamination of property. This record speaks well of the design of present-day medical sources, the efforts of source manufacturers to insure that only properly designed and manufactured sources reach the commercial market, and the careful use of these sources by the radiotherapist.

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OPEN DISCUSSION

Chairman: Norman Simon, M.D.

DR. SIMON: Since we have a big program this morning, questions about Dr. Pierquin's film will have to be restricted to 3 minutes each. The first question is about the anesthesia used for the different procedures. I noticed that the patient was not under general anesthesia, which is quite different from the practice in this country. Could you expand a little on the anesthesia used in the different procedures?

DR. B. PIERQUIN: We almost always now use a "neuroleptique." The patient is relatively conscious, he doesn't feel the pain of the needle. And that is better, particularly for old patients. Essentially the "neuroleptique" is sedation, a mixture of sedatives and tranquilizers. It's quite well tolerated by any patient and there are very few contraindications. But for tongue cancer we use a local anesthesia because we want to have the patient sitting. There's a special way of implantation for the oral cavity.

DR. MARTIN LEVINE (Boston): I'd like to inquire if Dr. Pierquin can give us some idea of local control and survival figures for patients with primary cancer of the breast.

DR. PIERQUIN: We are now working on a large series of cases, and I am not prepared to make a definite statement yet on cancer of the breast. We hope to establish the role of iridium in the treatment of early stages.

In tongue cancer, however, tumors of the mobile parts of the tongue, we now have about 150 patients treated for more than 4 years. In these patients, there were only 8 percent of recurrences. Most of them were controlled by local excision or new brachytherapy. Exactly 50 percent of these 150 patients have died within the period of 4 years and in these patients there were 2 or 3 local recurrences. But in the patients who have survived more than 4 years there has been no recurrence as of this moment. I think we have established that there is only a very small proportion of recurrence in tongue cancer treated with implants of iridium.

DR. NERVI: Do you know if you have any differences in success in treating tumors of the anterior part, as compared with the posterior part?

DR. PIERQUIN: Yes, of course.

DR. NERVI: And secondly, are the results in treating T-3 lesions of the tongue with iridium the same as in those treated with radium?

DR. PIERQUIN: No, they were quite different. The proportion of recurrence with radium at Gustav-Roussy was about 35 percent in the first year. But that was with inaccurate techniques of dosimetry. Now we get only about 3 to 5 percent of recurrence for the small tumor less than 4 cm. With good, accurate technique with radium, I think it is possible to have about 15 to 20 percent recurrences, but no less.

DR. KOTTMEIER: Dr. Pierquin, your technique is very elegant and I must congratulate you. I would like also to ask you a question. I used long needles with radium very carefully in the parimetrial tissue. We took films every hour, and found that the position of the needle had changed. Is it possible to avoid the changing of position of the material in the tongue?

DR. PIERQUIN: In our experience, the pins don't change. The tissue in the tongue is very firm. The hairpin shape of our iridium wire is also important in preventing change of position. We insert the pin into a muscular part of the tongue, where the tissue is quite strong. The miniaturized material follows exactly the contractions of the muscular part. When the metal pin is in the correct position at the end of the control with television, you can be sure that after 3, 4, or even 6 days it will be exactly in the same place.

DR. SNELLING: We were interested in the incidence of superficial necrosis that occurs when you implant the tongue with the epingle (hairpin). Could you dream up a substance that would perhaps give us an inactive bar? We wonder if one could make an epingle with platinum across the top.

DR. PIERQUIN: You get some necrosis, Margaret?

DR. SNELLING: Yes, I think you get necrosis at the point of entry because you have an active source coming all the way out to the surface of the tongue.

DR. PIERQUIN: I agree. When you look at the surface of the tongue after treatment, you observe some small transverse sclerosis corresponding to the active part of the hairpin. But in fact there is no real and durable necrosis here. It is an immediate reaction, which perhaps is a transitory necrosis. But the repair is normal in nearly all cases.

DR. SNELLING: Yes, I don't say it is important. But that's how we find it happens, and we did ask if they wouldn't make a needle where the top part of the single pin, or bar of the hairpin, was made of some material that wouldn't become radioactive, like platinum. But I think it would be a bit expensive.

DR. PIERQUIN: But the bar is very important, I think, for completion of the dose at the surface of the tongue.

DR. NORIEGA: I would like to ask Professor Pierquin what he does in cases with very dense tumors. We have had the experience in a few cases where we implanted a really hard tumor, very fibrotic and the wire bent even though we used the rigid guide.

DR. PIERQUIN: You mean when the hairpin is like that? Well, it takes a long time to train people in the hairpin technique of afterloading. It is much easier to train them in the techniques of Henschke with plastic tubing. It took Chassagne and me about 6 months of training technique to teach a student to place easily and correctly a hairpin in the buccal cavity and oropharynx. We also have instructed a group of students from all countries during the past 12 years.

For that there is a small trick. At the moment of insertion, your hairpin must be at a slight angle. But it is a problem, it is not easy to do the first time.

CHAIRMAN SIMON: Mr. Malaro referred to N-44, the ANSI Committee. It behooves me to state that it takes the American Standards Institute as long to promulgate a standard as it does to build a Hilton Hotel in Bulgaria. By the time the standard comes out we already have changed our methods of treating. We have started afterloading and remote loading without a standard. It is only by interchange at a meeting like this that standards and suggestions can at least get to people so there can be some action during the painful long wait between the planning of a standard and final promulgation of the printed word.

Dr. Moore had to return to Washington because of the pressure of work in Congress and in his office. He left with a suggestion that is indeed a mission for us: to answer a question regarding the use of radium. I have submitted this question to many of you, and I have some extremely revealing answers. The question is as follows:

For brachytherapy, should all radium be replaced by 1975?

I have a number of answers and comments which Dr. Boland will go over in a little while. Meanwhile, I would like a show of hands on three possible answers: Yes, it should be replaced in brachytherapy by 1975; No, it should not be replaced; and maybe.

(The question is put to the audience.)

CHAIRMAN SIMON: Well, it looks like the biggest category was maybe, which is no answer, I suppose. You will be interested to know that the answers which were written out, some with added comments, were about four to one in the "yes" category. At any rate, there are some very interesting answers which I think are appropriate, since they obviously were made by people who have given considerable thought to this question.

DR. BOLAND: The answers were overwhelmingly in the direction of the desirability of replacing radium at the earliest possible date. Hesitation as to the practicality of this step came mainly from the elder statesmen. If all radium were withdrawn suddenly, only a minority of the users would be able to change over to radium substitutes. And it's realized that the real enemy is not radium; it's ignorance, carelessness, and stupidity. Why change over from a radium hazard to a radium substitute hazard?

I was shocked to learn that over 2,000 nasopharyngeal applications are still performed annually. Now clearly we should do everything to encourage the use of radium substitutes and afterloading. But it's also recognized that everyone changing over has had some difficulty with a source: in its intensity, or linear intensity, or application. These are gradually overcome. We should also encourage the use of computer dosimetry for greater accuracy.

Now radium is something that will have to be phased out. But there are certain things that could be thought of immediately; for example, a ban on the import of radium into the country. Recall all radium plaques, since they leak. Nasopharyngeal applicators should be next on the list. If the government were to offer $20 a miligram for radium, quite a lot of people might go down into their cellars and find some of that two-thirds of the radium lost in this country.

So while the rationale in the questionnaires was, "yes, we must replace radium as soon as possible," there are notes of caution.

DR. SILVERSTONE: I firmly believe that all radium should be replaced as soon as possible. The risks involved are far too great. I don't know of anyone who hasn't experienced radium leakage. Surveys mentioned in yesterday morning's lectures revealed that leaking sources are very prevalent throughout the country. Anyone who has radium takes that risk, besides the risk of carelessness. When radium does escape, its consequences are intense and severe. Therefore, I believe that measures must be taken to get rid of all the radium in this country as soon as possible, replacing it with the much safer radionuclides, particularly cesium.

DR. VON ESSEN (San Diego): With regard to radium, I would like to suggest an interim use for the benefit of our good neighbors in the developing countries. Many radiotherapy installations there have a shortage of sources, a different situation, and a high prevalence of cancer of the cervix. We already have set up a small program of shipping radium to our neighbors in Asia, and hopefully in other places. So I hope that our affluent civilization, as it dumps radium, will supply it to others who need it.

DR. SNELLING: I'm a little doubtful about the ethics of exporting radium, just to improve the system in our own countries. (APPLAUSE.)

The only other thing I have to say is what I said in my original paper. In the United Kingdom we have all agreed that we should change from radium to cesium, particularly in gynecology. In implants we prefer to go to iridium. We agreed we should do this, but there are economic factors. Our chief trouble is our recovery charge, and I hear that this problem exists elsewhere. If that were to be covered, then I think that all centers would change over quite happily. But at present we have to pay to get rid of our radium. That is our chief trouble.

Another point, I don't think we agree entirely with Dr. Silverstone that we must change at once because of dangers. We have large centers that have used quantities of radium for a long time, and where the dosage received by the staff is entirely satisfactory. We do not say they must change straight away. But centers where the handling of the radium is not satisfactory, and new centers, we felt, should have the cesium at once.

MR. PARKER: My comment is not very different from that of Dr. Snelling. I consider it insulting to inflict radium on our colleagues in the developing countries. We already have made that mistake with x ray machines. The good ones go to skilled people, the castoffs are sent to those who have not had equal opportunities of training. It should be the reverse. Those with less skills should have the most suitable weaponry. For the time being, if necessary, let the more skilled people muddle through with the older devices. (APPLAUSE.)

CHAIRMAN SIMON: I would like to point out that Mr. Parker's and Miss Snelling's comments were voiced by others in the written response, and we're grateful, I would also like to quote from Mr. Parker's comments in writing: "Radon seeds should have been outlawed some time ago."

DR. SUNTHARALINGAM (Jefferson Medical Center, Philadelphia): Throughout these 3 days I have found it very disturbing that nothing was said about the problem of specifying the source strength of radium substitutes. In various presentations, mostly by our clinical colleagues, we heard of units such as milligram radium equivalents and millicurie per cm. Milligram radium equivalents, the conventional unit for clinicians with years of radium experience, is a very misleading unit. My fears that it is being misused have been confirmed this morning by certain statements made by the commercial representatives. I would like to pose questions to some of the dosimetry specialists who were here yesterday, and to Dr. Snelling, as to what their thinking is in terms of specifications of radium substitute sources.

DR. ERJAVEC (Ljubljana, Jugoslavia): In 1960 in our radium department we had a nice old little prosthetic fellow who dismantled a radium tube of 8 milligrams, and it cost us $70,000 to clean up the mess. Therefore we are voting with both hands for replacement. (LAUGHTER.)

DR. NERVI: Do you mind if I pose a question to Dr. Pierquin, Dr. Henschke and Dr. Chassagne? I'm not speaking of radium protection problems, and shielding is not my particular problem. I'm a clinician, and I want to pose a specific question. (DRAWING AT BLACKBOARD). Let's say you have a T-2 NO infiltrating carcinoma of the posterior third of the tongue. How do you treat it -- with radium or radium substitutes? And if you treat this patient with radium substitutes, which kind of substitute, and what results do you get?

DR. PIERQUIN: My answer is very brief. If it is not too infiltrating, I would use hairpins of iridium. If infiltrating, I would use Henschke tubing.

DR. HENSCHKE: I would treat this lesion first with external therapy and see how it responds. If it does not respond well after 3,000 rads, we would implant with loops of plastic tubing containing iridium.

CHAIRMAN SIMON: I would treat this with great humility. Externally, I don't think you have a curable disease. I'm afraid that there wouldn't be much yield by implant.

DR. BOLAND: I think this is one that should be treated by external radiation alone. It is technically too large and too difficult for interstitial implantation. Dr. Pierquin does not agree.

DR. PIERQUIN: We have had 17 percent recurrence in about 100 cases of this type of lesion. But I agree with Dr. Henschke in first using external radiation up to 3,000 or 4,000 rads. After that we would use interstitial iridium, or perhaps chemotherapy. Perhaps even chemotherapy by intraarterial methotrexate, followed by implant.

DR. ERJAVEC: In our institute it would be intraarterial chemotherapy first, and there is a 50 percent chance the tumor would disappear. Regardless of the effect, the lesion would be given full radiation treatment: external treatment, then implantation.

DR. HILARIS: I would like to consider the T-3 lesions. Our experience has been that we cannot control this tumor with interstitial radiation. In these large lesions, we depend largely on external radiation therapy.

DR. NERVI: We all agree that to control this disease we have to give external radiation and interstitial radiation. I have had a lot of experience with chemotherapy in this lesion, and the results have been poor.

I would say that if you want to implant the posterior tongue interstitially, you must do it with a rigid needle, a radium needle. You would never be able to do it well with the flexible wire or tubing. I think that the work with iridium is extremely important, because it has helped us to be more accurate and precise. But in this tongue location, we or at least I haven't been able to control tumors. We had 90 percent local recurrence with hairpin, much less with radium. You can implant radium at this site, and you can also use a radium substitute. So, I don't think that radium has to be thrown away. Let's use more shielding, and let's try to find something else, because at the moment in some lesions radium cannot be substituted.

DR. MARY NELSON (City of Hope): Dr. Nervi, what you're really saying is that you like rigidity. Isn't it just possible to get a radium substitute in a rigid applicator?

DR. SAHATCHIEV: I don't know if I am the representative of a developing country, or not. But in Sofia, we changed from radium to cobalt in 1954; now we are changing from cobalt to iridium and tantalum for interstitial therapy, and to cesium for intracavitary.

DR. VON ESSEN: I think I'm being shot down in flames, but I would still like to repeat my remarks. There is safety, with the proviso that radium sources are carefully standardized, examined, and well sealed in afterloading devices so that their safety can be maintained over the years. I still think it's an important point from the standpoint of humanity that we do something to provide radioactive sources for the treatment of cancer, and I think this is one very useful way of doing it. I agree it is in a sense giving away what we now think of as an inferior product. But it is a useful surplus product, that's the important thing.

DR. SNELLING: We did feel that as an interim measure, until we all have our cesium, manual afterloading with sealed radium might be permissable.

CHAIRMAN SIMON: If we may go to another very important and exciting topic, californium 252, it seems that there are two important questions. I have alerted Dr. Oliver, since Dr. Atkins had to leave, to answer the two questions. The questions are: How do you get californium? What facilities do you need as far as personnel shielding, and neutron instrumentation are concerned?

DR. OLIVER: Well, you've asked two very important questions. Californium is a product that will probably not be used in every institution. The only institutions that should get it are those that have qualified personnel with clinical experience in interstitial and intracavitary treatment, and the staff to back them up in the physics problems. This probably entails the use of a physicist trained in neutron physics. It's evident that most medical physicists, and probably some health physicists, are not experienced in neutron dosimetry and neutron physics. So what you need is properly trained personnel from the physics, clinical, and radiobiological standpoint. And that brings up the second thing: you also need a frame of reference on the radiobiological parameters. What clinical RBE should you apply to get the treatment dose you think proper from your experience with radium?

As far as proper equipment is concerned, you have a different animal on your hands. Neutrons are not the same as gamma rays. They cannot be approached in the same manner. They are much more dangerous, as Dr. Atkins and I pointed out yesterday. You've got to have hydrogenous shielding, lead will not work. This entails expensive new fabrication, so you should have some capital behind you.

Hopefully, the techniques would not be changed. The source geometries would be similar to what you might expect with iridium 192, or perhaps cesium tubes. I don't advocate direct loading of needles, which is a dangerous proposition. You've got to have personnel monitoring; film badges have not proven adequate, not even neutron film badges, let alone conventional gamma-ray badges. Two institutions in the U. S. are developing TLD neutron badges, so this may be the answer.

In my opinion, you shouldn't use californium without computer dosimetry. You've got to calculate not only the gamma ray but also the neutron dose distributions, and they are somewhat different. You've got to consider both of them in combination to get biologically effective doses. You've got to give considerable thought to what the AEC has termed "human radiobiology." It may be unfortunate terminology, but in the first phase of the program that's primarily what we're talking about.

Afterloading techniques are vitally necessary for the application of californium.

Now your first question, I believe, was how do you get californium. The AEC has developed advisory committees, and they have had the cooperation of NCI in the form of the committee on radiation therapy studies. These two committees act jointly in advising manufacturers how to distribute the sources.

The program, as presently set up, has selected about 13 institutions that have shown superiority and competence in radiotherapy and physics not only in the U. S., but also in France and England, perhaps in Australia and Japan. They have the staff required to do the clinical work as well as the physics. A proposal must be submitted to the AEC covering all the aspects that I've mentioned, explaining in detail how the problem will be approached, maintaining safety of both patient and personnel and at the same time getting meaningful clinical results.

The important problem here is, how are you going to get meaningful clinical results? We've been working on a program for 3 years. Last year we implanted just 18 patients. If each institution implants twice that number, they still will not get an answer for 10 years or more whether californium is better than radium. So you've got to have a collective agreement between the institutions, probably one based on a common dosimetry system and selected radiobiological parameters.

It's not an easy question, and it's going to take lots of work. But if we can believe the radiobiological data we've seen thus far, californium may well prove to be more effective than radium.

CHAIRMAN SIMON: The next topic that I'd like to take up is the important one of specification of dose, and specifications for iridium 192 sizes. That is what Dr. Henschke brought up. You will recall, he said that iridium sources are available to him at Howard University from Saclay in France and Sorin in Italy. Yet they are not easily available to us in the U. S. Dr. Henschke, who has been thinking of this problem, has been trying to resolve it.

DR. HENSCHKE: I showed those drawings, and I think we might use them as reference. The source we mainly use has a diameter of 0.3 mm. The iridium core is enclosed in stainless steel of sufficient thickness to completely absorb the beta radiation. That's the distinguishing characteristic of this source; without stainless steel there is no beta absorption, the surface dose from betas is at least 10 or 20 times higher.

Now then another source is very similar to Dr. Erjavec's in Ljubljana; in fact, I believe we supplied him with his first sources. That too is a stainless steel tube, with an iridium core. His needle is slightly smaller in diameter, but you could make it the same diameter readily to filter out completely the beta radiation.

These sources would make it possible to provide what Dr. Snelling wanted, a hairpin which has no activity in the crossbar. You can make a great variety of other configurations.

Other sources are available from Saclay, one with 0.5 mm diameter containing a core with a diameter of 0.3 mm. It is used mainly for the hairpin because it has greater stiffness. The iridium in the nylon tubes (Squibb type) has a smaller diameter. In both cases, beta radiation is, to all practical purposes, filtered out.

The hairpins, as some of our speakers brought out, are a bit soft; I think the stainless steel pins of the same size are much better. Stainless steel normally is very stiff, of course; but by tempering it in the flame, we can get almost any degree of stiffness.

I'd like to have Mr. Malaro's comment on another problem. In some types of iridium sources it is left to the user to cut them to size. The cutter pinches the iridium alloy; it's very hard, and gives very little contamination. But if you use sharp scissors and very sensitive methods, you could be able to demonstrate some contamination on cutting other sources. We never got a completely satisfactory answer from the AEC, whether they regard cutting as opening a sealed source. Actually, such sources can only be called semi-sealed; I think a clear statement from the AEC would help us in further development of those sources. They could be sealed better, but that would greatly increase costs.

As far as cost is concerned, stainless steel is of course less expensive than platinum. However, the sources we make are only a little cheaper, for the major cost is labor.

Another point I want to bring out is that round sources are very easy to handle in a hopper, but cylindrical sources are very difficult to handle in an automatic device. The numerous attempts to make a bore with an iridium core and steel covering to filter out the betas (which we still think is quite important) have turned out to be prohibitively expensive.

In our present status, the sources for intracavitary radiation — cesium and radium -- are quite satisfactory. We are still merely in the development stage for interstitial sources. I personnelly am in favor of the idea that we have one radioactive material, one little unit which we can lubricate and activate in great numbers very inexpensively. The reason such sources are not readily available is that there is no consensus from the scientific and commercial point of view.

MR. MALARO: Well, Dr. Henschke, I'm afraid that you've hit our Achilles' heel. I'm not sure that I can give a direct answer to your question. I think this is one of the areas where work needs to be done on standards for sources. It's fairly easy for an encapsulated source, there are standards; but there are no set standards for unencapsulated sources.

As far as the AEC is concerned, we would be willing to consider this or any other type of semi-encapsulated source for use in radiotherapy, providing that Dr. Henschke can show us that this source, when cut will provide only very slight contamination, say in the thousandths of a microcurie. On the other hand, I think each using physician or institute would have to show the expertise and equipment necessary to cut these sources to keep contamination within the designed limits.

Now I'd like to put in a plug to Dr. Simon and other people who are working on standards. This is one particular area where little or no work has been done. There is very little evidence based on the use of these sources, and I'd certainly like to see some work done by people in this particular industry to develop standards and criteria for the use of these semi-sealed sources.

CHAIRMAN SIMON: For the past 3 years in the Mount Sinai Hospital we have been using the miniaturized cesium sources in Vycor glass described by Dr. Silverstone and myself, in the treatment of cancer of the cervix and fundus of the uterus. Wipe tests of these devices show no removable contamination. The porous glass rods are within stainless steel tubing.

MR. JAMESON: In the United Kingdom, we are using iridium to a considerable extent. It's made by Harwell to a similar dimension as Saclay's. At the last count, a few weeks ago, there were about 10 centers in the United Kingdom using iridium wire for needle implants.

CHAIRMAN SIMON: Can you answer the question Dr. Henschke has posed regarding the possibility of contamination at the cutting point?

MR. JAMESON: We have no comments on that, at the moment.

DR. PIERQUIN: We have tested a lot of wires with scissors, and there is no contamination when we cut wire. The reason is that with a scissor cut you indent the platinum and close it over the iridium core. We have done this under a microscope, to be sure; each time the platinum covers the active material inside. Our French Atomic Control Commission performed about 1,000 tests with wire to see if there really was contamination, and they didn't find a picocurie. For this reason we now use iridium wire all over Europe.

The most important thing is to reach common agreement on the basic size of the wire. I think the smallest wire should have a diameter of 0.1 mm of iridium in an envelope of platinum, 0.3 at most. This is the smallest size that can be fabricated easily, and perhaps it should be the basic unit throughout the world. If we agreed on a 0.3 mm diameter, I think it would be useful since it is the standard size in Europe.

DR. SUNTHARALINGAM (Jefferson University): For the past 18 months we have been purchasing iridium sources from Saclay through a distributor in New York. During the past three months there has been a misunderstanding; therefore there no longer is a U. S. distributor. But you can get these sources directly from Saclay. We have a standing order for delivery every two months, and have encountered no difficulty whatsoever.

Now regarding leakage, I'm not too sure whether this is properly understood. The AEC wants to know if there's any radioactivity leaking from the source after you cut the wire. Leakage occurs only if an inexperienced handler tries to cut the source. Some clippings may be radioactive, but this type of activity is very low; in fact, it can be detected only with very sensitive instruments. But once you cut the source, it no longer is leaking.

CHAIRMAN SIMON: I'd like to ask Mr. Malaro a very important question, for those of us who might want to order something from Saclay: is it acceptable to purchase this material in states which do not have enabling legislation?

MR. MALARO: It most certainly is. You can purchase radioactive materials anywhere, either in the United States or abroad. However, if we have not evaluated the particular materials you purchased, it is your responsibility to submit to us sufficient information to show that you are capable of handling this material, or that the material has characteristics that make it inherently safe. The responsibility is on the user in this particular case.

CHAIRMAN SIMON: Have you evaluated Harwell's, Saclay's and Sorin's iridium?

MR. MALARO: No, we have not. Let me qualify that. There are people in this country who are using it, and we have evaluated it partially on an ad hoc basis. For example, when an institution wants to use it, we evaluate it in the context of the ability of that institution to handle it. We have not evaluated it to the point that we will allow widespread distribution of this type of material in this country.

CHAIRMAN SIMON: May we pursue this further by getting a prototype organization of radiation control in the United States, outside the AEC. I'd like to ask Mr. Blatz: Can we in New York City order Saclay iridium without making application for nonroutine use and showing it is safe?

MR. BLATZ: We have agreed to keep our program compatible with that of the AEC. So whatever the procedure is for the AEC, it would be the same for any state that has an agreement with the AEC. You'd have to present some evidence that it can be used safely.

CHAIRMAN SIMON: The next problem has evoked a number of questions, and we are very fortunate in having a well-known representative of the ICRU to discuss it. The problem is: How do you specify the activity or strength of these radionuclides? Dr. Bernard Pierquin and many others have been thinking of the problem of whether to specify iridium in milligrams of radium equivalent, or mCi of activity. What gamma ray output figure do you use in defining such activity?

DR. PIERQUIN: When we receive material from Saclay, the strength is always specified in millicuries per cm. Because in working with wire we always need to know the activity per cm.

DR. CHASSAGNE: The millicurie is an international unit. Why don't we all use the millicurie instead of the milligram radium equivalent, which is a silly unit?

DR. SUNTHARALINGAM: Since we have been interested in this problem for the past 18 months, and haven't come up with a solution, I'm going to pose the question over and over again: What do we want to do? I agree that the ICRU has recommended that the unit of activity be the curie or the millicurie, but please tell me this: How are we going to accurately measure millicuries?

I'll give you the reason why I raise this question. For the past 18 months we have been assaying shipments from Saclay. They tell us, their assay is plus or minus 5 percent. Discrepancies existed in assays of activity in earlier iridium sources obtained from Squibb (Dr. Henschke's preparation). Differences of 20 to 25 percent were now observed between the assays obtained from Squibb and the activity specified by Saclay.

Not knowing whether this was due to some discrepancy in our instrumentation, I corresponded with Saclay. To my surprise, I had a reply saying that they had detected a change in calibration of 10 percent, and they gave us new calibration factors. We still are inconsistent, anywhere from 5 to 15 percent. Now for uniformity in specifying the dose to the patient, we continue to use the assay of activity as determined at our own institution.

I also am interested in doing in vivo dose measurements. We have a lot of experience in thermoluminescence dosimetry. There is disagreement between calculating the dose using millicuries, as determined by an assay, and the actual dose delivered to the patient. In using millicuries per cm, you have to use the specific gamma-ray constant for the particular isotope. There are uncertainties in the specific gamma-ray constant for iridium 192; it varies anywhere from 4.8 to 5.5 in the various publications. When I asked Dr. Dutreix, in our correspondence, the IAEA committee came up with 4.8 as the best available number. The ICRU handbook in the U. S. reports 5 as the best number. Here we have a 5 percent difference. I think we are cheating ourselves by giving isodose distributions to accuracies of 1 percent to the clinician. He looks at the figure: 40 rads per hour. But are we treating to 40 rads per hour?

DR. LOEVINGER: Clearly this is a very important question. I suspect that the possibility of really getting rid of this terrible stuff, radium, depends upon getting a satisfactory, widely-accepted answer to this question. In trying to solve any important problem, such as this, one should look for first principles on which to base a decision. I suggest that the chief principle is this: We should try to find a method of specifying the strength of radium substitutes which will preserve as much as possible the vast clinical experience with radium that has accumulated.

The use of milligram equivalents of radium is a superficial way of doing this. It appears at first glance as if you are equating the sources with radium sources. I think, however, that this is a deception. The word equivalent should always put you on your guard. Two different things may be equivalent in one respect, but they cannot be equivalent in all respects and still be different, and this milligram equivalent of radium refers, I think (but am not sure), to exposure rate at a certain distance. But it is certain that other types of sources, cesium and iridium and so forth, are not equivalent to radium in terms of the dose distribution around clinical sources.

Now let me suggest a way to preserve the clinical experience with radium. I'm not sure I can give you the best answer, but I'll just sketch the answer that comes to mind after listening to these learned talks.

First of all, I think that one should use modern techniques to describe as accurately as is necessary the true absorbed dose distribution around favorable radium sources, or favorable radium distributions. You must try and put your radium experience into meaningful units, into a form meaningful to other people. I think this can only be done in terms of the distribution of absorbed dose around the clinically important and useful radiation distribution.

Then, we must try to specify a radium substitute in such a fashion that it can be used to produce the same desirable dose distribution. To do this, I'd say that it is unnecessary to bring in activity. The use of activity units may be useful, but this is only a stratagem. I believe it is not necessary to specify activity disintegration per unit time; it is really irrelevant to the radiologist. What he is interested in is the absorbed dose.

I believe the sensible way is to specify your sources in terms of exposure rate under a given set of circumstances, such as R per unit time at a certain distance in air. In my brief talk yesterday I tried to say that all the necessary physical information is now available. Take any radio isotope, any radionuclide source you have in mind, with any kind of encapsulation. All the information you need to specify the distribution of an absorbed dose in tissue around that source is now available.

There is no magic in radium, it is simply a habit. We can take any other sources and use them in a way that will produce the same desirable dose distribution that you have learned by experience to expect with radium. It is my impression that the best way at the moment would be to specify activity in radiological units, in exposure to unit time at a stated distance.

I suggest that this is the kind of problem where agreement is needed. It doesn't do any good for me or any other person to decide it; you need agreement between the source manufacturer, the consumers - that is to say, the clinicians - the Public Health Service people, and the Bureau of Standards who must do the calibration. I would think it very appropriate that the Public Health Service or someone convene a gathering of representative groups and try to arrive at a decision which all can accept.

DR. HENSCHKE: To put this problem in perspective, when we first introduced iridium sources in 1953 the value in R per hour per centimeter varied anywhere between 2.3 and 5.5. The reason, of course, is that iridium has a very complex spectrum with 12 gamma lines. We calibrated these sources against the cesium or radium standards, and we probably should have called the unit an exposure rate. But at that time everything was so new, that's why we picked the milligram radium equivalent. I think it has served very well. What we need to hear from Dr. Loevinger now is, what is the best value for the gamma-ray output of iridium 192?

I think we should not switch to an exposure unit because finally we have to switch to millicuries. We are forced to specify activity in millicuries for shipments and license. What should be done is no problem for cesium, which can now be specified in millicuries. I think we should give all values in millicuries now, there's no reason anymore to use milligram radium equivalent. There's a very fine factor of 2.5 between radium and cesium.

But we need a conference to decide on that, the ways are different in the U. S. and Great Britain, for instance.

MR. PARKER: One of the committees of the NCRP -- the Chairman is Dr. Marvin Williams -- is preparing recommendations on the preferred method of making some of these standardizations. I think there could be a valuable interchange between that committee and those such as yourself, Dr. Simon, who will be putting to practical use the proceedings of this conference.

DR. ERJAVEC: May I explain how we approached the problem with iridium 192? Our dose distributions around linear sources are made with a gamma factor of 5. We assume that we have a source of gamma factor 5, and measure our iridium wires in a calibrated ionization chamber. If we have made a mistake in the controversial gamma factor, we can correct back in using it so that we don't make mistakes in the dose. Thus we confine our mistakes to specification of linear activity.

MR. BLATZ: Regarding cobalt teletherapy sources, I should mention that about 5 years ago we adopted a change that made us slightly incompatible with the AEC. They have always licensed teletherapy sources in terms of curies; we license teletherapy sources in terms of RHM (R per hour at a meter's distance), an unconventional but widely used unit. All dosage and all protection calculations are related to RHM, rather than curies.

DR. PIERQUIN: In France and England, control and calibration of the active material is the responsibility of the user -- the department of radiotherapy and the radiophysicist. The nuclear center routinely gives us a rough approximation of the activity; we must ourselves establish the precise activity of the material in curies. Secondly, and not routinely, the nuclear center provides us with an accurate calibration. But that is very expensive. I must repeat, according to French law the final responsibility is not with the nuclear center, but with the user of the material.

CHAIRMAN SIMON: The next subject we will take up because of its importance, and your desires as expressed in these questionnaires, is the standardization of dose in cervix systems. As an introduction, I would like to use that which we requested from Dr. Hilaris. He has specific data concerning reactions with rapid dose rate, which I think are pertinent.

DR. HILARIS: Remote afterloading using high intensity cobalt 60 sources was introduced at Memorial in 1967. Each source is cylindrical in shape and measures 1 x 1 mm. It is enclosed in a stainless steel capsule that measures 10 x 1.7 mm. Each capsule is attached to a stainless steel cable which permits advancing the sources from the safe to the treatment position by either manual or automatic control. The remote afterloading presently is used in the routine loading of applicators for irradiation of the vagina. It also has been used in patients with cancer of the endometrium or the cervix.

Intracavitary vaginal irradiation was used in approximately 60 patients. About one-third of these are available for a two-year followup. We used approximately 3,000 to 4,000 rads on the surface of the applicator, depending on the size of the applicator. The applicator is cylindrical, of various diameters. The basic difference between conventional radium and remote afterloading is that the radium was given in one application, whereas remote afterloading is given in 3 applications of 500 mg hr each, spaced at two-week intervals. The entire treatment takes about four weeks. If treatment is given for curative purposes, external radiation therapy is added to the intravaginal radiation. Early evaluation of these patients has shown no unusual reactions. A detailed report will be forthcoming.

Preoperative intracavitary uterine irradiation was used in 20 patients with endometrial cancer. Most of these patients were Stage 2. The applicator utilized was of a bouquet arrangement with 3 tubes permitting the afterloading. One tube was placed in each cornua, the third in the center. The computer can reproduce a uniform dose of approximately 4,000 to 5,000 rads around the tubes. This corresponds to about 3,500 to 4,000 mg Raeq hours, and it was given in about 1 hour. Hysterectomy was performed 4 weeks later. Gross effects on the uterine specimen were similar to those obtained with radium given at a slower rate. Microscopic examination, however, showed more intense fibrosis and a very few atypical glands lined by a few epithelial cells. These changes are more severe than those obtained with radium, even though the mg hr of exposure were the same. Obviously, dose rate played a role here.

The last group of patients consisted of about 40 patients with cancer of the cervix, treated in 1968 and early 1969. Five patients had one uterine application, using Henschke's applicator, of 2,000 rads to point A; this group did not show any unusual reactions. Fourteen patients had two uterine applications, 3 weeks apart, of 2,000 rads each to point A. These patients did not show any unusual reactions in the first 5 to 6 months after treatment. Six to 9 months after the treatment, however, late reactions appeared, including damage to the small bowel in two cases. The remaining patients had 3 uterine applications of 1,500 rads each, spaced 3 weeks apart. Although this group did better than the previous one, the late reactions were still more prevalent than in patients treated by conventional dose rate radium therapy.

Pending further laboratory investigation relative to dose-time relationships, the remote afterloader has been utilized in the past 2 years only in intracavitary vaginal irradiation.

CHAIRMAN SIMON: We thought it would be important to make this information a part of the record in discussing not only dose rate, but also the problem of points A and B. How do you specify the dose in the intracavitary treatment of carcinoma of the cervix, points A and B apparently not being so important now. The same question applies to carcinoma of the corpus.

DR. KOTTMEIER: That is a very difficult question to answer. But first of all, we have to agree that points A and B have no relation to dose distribution, nor to the disease. Such applications as we saw here in Dr. Hilaris' cases are rarely used with radium. What we should do is examine the patient under anesthesia; thus it's possible to tell whether there is central disease, and you can plan with the following dose determination:

The dose to the bladder, the rectum, and 4 or 5 cm from the center of the disease will be the basis for the studies. It is very easily done in each case, and yields information on the dose distribution from intracavitary radiation. If you have the facilities of a computer (which we don't) it's much easier.

DR. CHASSAGNE: I think the problem is very important because now with computer calculation we are starting a different way of displaying the data. Next year we will start to use the oblique lymphatic plane described by Dr. Fletcher.

Some of us do not choose this, we use volume. For instance, we say we have treated a cervix cancer with a volume of 50 cc irradiated at 6,000 rads. Others prefer not to use volume specifications. And some specify the dose in the bladder at the surface of the catheter, others do not; we specify the dose to dead seeds implanted inside the cervix, anteriorally and posteriorally.

I think we should give some thought to dose specification, because in a few years none of us will understand what the others are doing. In the past we had only two ways of talking to each other: we said "milligram hours," or so many rads to point A and point B. But now, with the computer, we may have no way of understanding each other. It will require a lot of time to settle this problem.

Our group of brachy radiotherapy (we call it curie therapy in France) is going to meet next week with Dr. Sahatchiev, Secretary of the European Group of Curietherapists in Bulgaria. We agreed two years ago to specify the dose to volume receiving 7,500 rads. That means to specify the dose to the surface of an isodose curve of 7,500 rads, and to identify the length, thickness, and width of this isodose curve.

DR. HILARIS: It seems important to measure the dose to the primary tumor and to the pelvic nodes, which will vary with the level of the nodes. This can be done only with a computer. Although it is important to specify the dose to the rectum and bladder, we found that was not enough. We had acceptable levels of dose to the rectum with radium, but when we visualized the sigmoid we saw that it actually sat on the top of the fundus. It's not enough to specify the dose in the lower part of the rectum alone, we should also measure the dose higher up. Of course the volume is important, as Dr. Chassagne mentioned. Then, how do you combine the dose with external radiation therapy? I confess we were not really able to find an acceptable solution in the individual patient.

DR. SNELLING: We have computer dosimetry, and this of course has revolutionized the whole problem. Before then, we used points A and B. If one had the knowledge, it was just a handy way of comparing one technique with another, and one case with another. With us, the treatment of any patient depends on knowledge of the computer dosimetry. One automatically considers the uterus, the glands, and various other structures.

The development of an absolute system for coding cases also seems a matter of immense importance when you compare one technique with another. Here we would accept the definition proposed by Dr. Chassagne, and the work of the European group of radiotherapists.

You were asking about multi-source treatment of carcinoma of the fundus. In our center, we use computer dosimetry. We have taken a line that in fact was 0.5 cm outside the sources, and used that block of tissues.

DR. ROSWIT: The computer is great for sources that are large and not too many in number, because you've got to feed it the precise position of each source in space, in rectangular coordinates. But you can't do this when you have multiple small sources, at least I can't. At Memorial they have Eagle Eye, who's a master at this, and they have that elegant digitizer; but we ordinary folk can't do this.

So we can't use the computer for multiple sources. Ten years ago we adopted the technique of taking a direct measurement in the patient, and this I think is the most realistic approach. As a clinician, I am interested in the vital points—bladder, rectum, and pelvis—as well as the head, neck, mandible, great vessels, and the eyes. Only direct measurement gives you the truth for each patient, rather than an elegant display of figures on a piece of paper.

I'm concerned with the patient at risk, so for more than 12 years now I've been exploring and employing solid state materials to develop miniature dosimetry systems. We finally have done this, and we've used them in several hundred patients. We use silver activated glass rods in a gold shield, needles, tubes, and a whole array of catheters and devices for getting into every organ of the body. We've done this in several hundred cases now. We've gone on to thermoluminescent calcium fluoride, lithium borate, and lithium fluoride—again permanently encapsulated in glass. We put them everywhere to supplement and check on the computer.

DR. KOTTMEIER: In order to compare techniques, it is necessary to specify the dose. We know all isodose curves around the various applicators we use. But if we do not specify one special point, it is impossible to compare the various techniques. Whether you use 2, 3, or 5 cm doesn't matter. But if you use the tumor as a central point, and take 3 or 5 cm from the tumor, it is possible to get some visualization of dose distribution.

In addition, we should measure the doses directly in the bladder and the rectum, then we will have even more information about dosage distribution. The trouble is, when you read in papers that they gave so much external radiation, and so much intracavitary radiation, and mixed them together, you learn little about the actual dose.

DR. BOLAND: In intracavitary radiation, the dose at specified points is very important. A general statement of dose is really one of the envelope systems; the allowable dose depends on the size and shape of the envelope. A single source would have a spherical envelope; when there are multiple sources, it becomes symmetrical; a linear source gives a long, sausage shape. We should end up then with a nominal dose of say 6,000 rads, and if it's a spherical shape the computer can tell us the number of cc that receive this dose. Presumably the tolerance is different when we get to irregular shapes, but eventually the computer may be able to give us the spherical equivalent volume to which this dose is delivered.

DR. SILVERSTONE: I would like to continue with what Dr. Boland has just described. I think that point A was one of the greatest advances made by the Manchester group many years ago, and it still is extremely useful until computers take over. Now point A does not represent a point to me; it represents a volume that is roughly pear-shaped in the transverse plane, and somewhat oval in the saggital plane. We know from experience that all Stage I and many if not most Stage II carcinomas of the cervix fit into this pear-shaped volume.

Dr. Loevinger and I demonstrated over 10 years ago, by use of Adlux film, that even with angulation of the tandem on the colpostat and other variations, the pear-shaped isodose contour still followed the distribution of the disease in Stage I and in many of the Stage II cancers. At least for those cancers we have valuable information which we can use until computer technology takes over.

DR. KOTTMEIER: I am sorry that I must disagree with Dr. Silverstone. Only in a few Stage I cases is he correct. In early Stage II carcinomas the dose distribution may be quite different on the right and left side. In all our measurements, the paracervical triangle is assymmetrical.

DR. PIERQUIN: In my opinion, it is very simple. The only problem in dosimetry is computer or no computer. If you have a computer, you have an anatomic view of any plane; if you can relate the anatomy to the tumor, you know where you want the dose. If you have no computer, you have no real dosimetry.

CHAIRMAN SIMON: Thank you. We have remaining questions and topics that would take us until six o'clock tomorrow morning. We are honored to have the last two speakers, Dr. Kottmeier and Dr. Pierquin, on this program. We are also so grateful to the wonderful speakers who presented such remarkably fine material. It will be a real challenge to us to get it down in black and white, including the discussion, and make it available to you. Although the audience was exceptionally large, its quality was high, and to them too we are indeed grateful.

DR. JOHN BOLAND: We thank all the visitors who traveled so far to make this conference a great success. And the final thanks goes to Norman Simon for his idea of having the conference, and for his smooth organization which has provided us with a most enjoyable and profitable three days. Thank you, Norman. (APPLAUSE.)

DR. KOTTMEIER: I must tell you, I have been to many conferences in the past few years, but this is the finest conference I have attended. I learned very much from it. (APPLAUSE, AND THE MEETING WAS ADJOURNED)

SUBMITTED LETTER

DR. W. S. LOWRY (Portland, Maine): In the discussion on pelvic dosimetry for carcinoma of the cervix, Dr. Silverstone rightly noted that points A and B have served us well in the past and should not be discarded lightly. Dr. Kottmeier recommended that the dose be specified in the bladder and rectum and at a distance of 5.0 cm from the center of the tumor. Dr. Boland (and others) advocated quoting the volume enclosed by an envelope whose surface dose is 7,000 rads. Earlier in the conference, Dr. George had been using a modification of the Ellis Formula to give the dose at point A as 2,500 rets. Dr. Suit discussed Liversage's alternative formula.[1]

I believe we now have a unique opportunity, after 30 odd years, to combine all of these concepts on the computer and, at the same time, incorporate the most up-to-date thinking in radiation therapy, radiobiology, and radiation physics. In the final analysis, when we come to compare pelvic dosimetry in different centers we will need to know not only the dose at a fixed point, but also the volume of tissue irradiated and the fractionation used. In most clinical situations throughout the world a dose of 2,000 rets is considered lethal. For this reason, I would recommend that we quote the volume of tissue enclosed in the 2,000 ret envelope. This envelope would still be a "flat pear" whose "waistline" would lie somewhere between points A and B. It would also be somewhat closer to Dr. Kottmeier's arbitrary 5.0 cm point.

The 2,000 ret envelope incorporates time and is, in effect, a 4-dimensional concept.

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[1] "The values of the (fractionation) exponents are reasonable. . . . and safe in clinical application. . . . . So many new observations or experiments would be needed to establish valid alternatives, that different values are unlikely to justifiable for many years to come." Fowler, Ellis, Liversage. Brit J Radiol, Feb. 1971, p. 89.

APPENDIX: PRESENTATIONS BY COMMERCIAL SUPPLIERS

MINIATURIZATION OF MONOLITHIC CESIUM 137
BRACHYTHERAPY SOURCES AND AFTERLOADING APPLICATORS

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HISTORY

During March, 1970, the Atomchem Corporation purchased a nuclear laboratory from the Atlantic Research Division of the Susquehanna Corporation. In addition to normal laboratory equipment and supplies, several patents and patent applications were acquired. The most important of these from a source-manufacturing standpoint deals with the entrapment of radionuclides in a porous glass inert matrix. This radionuclide-porous glass concept has been the basis of our success in miniaturizing brachytherapy sources.

In the transferred records we found an indication that Atlantic Research had supplied Dr. Norman Simon at The Mount Sinai Hospital in New York City, with cesium 137 brachytherapy sources. While we have been supplying strontium 90 beta applicators for medical applications, our first meeting with Dr. Simon pointed to the need for miniaturized sources (1).

Miniature source integrity has been demonstrated in over 2 years of use by Dr. Simon, source wipe-test data showing no increase in removable contamination. The Atomchem sources are identical to these allowing for mechanical improvements introduced by Dr. Simon.

GLASS CANES

The backbone of our sources is the monolithic porous glass (Vycor) cane. The cesium 137 is in solution of a predetermined concentration. The canes, 0.8 mm in diameter, are cut to length, cleaned and dried, and put to soak in the cesium solution. The pores of the glass are cavities 25 A. U. in diameter, continuous throughout the cane; these become filled with the cesium solution. The canes are removed, cleaned, dried, and fired at a temperature over 1,000° C., causing the cavities to collapse and entrap the cesium 137. The firing causes the canes to shrink linearly 10 percent. The fired canes again are cleaned to remove residual surface contamination, dried, and finally encapsulated.

The fired, cleaned, unencapsulated canes have been checked to determine leachability. This would be of interest in the unlikely event an encapsulation weld failed. The leachability of the radionuclide in colution after soak is only 0.004 percent. [The limit specified in USASI, 1968 is 0.01 percent (2).]

SOURCES

We encapsulate the cesium 137 canes in 18 gauge 304 stainless steel hypodermic tubing. One end of the tube is welded closed with tungsten inert gas (TIG) and checked for leaks. The cane is inserted through the open end, followed by a stainless steel plug. The end is closed again by TIG welding, and the inactive handle is attached. This technique is used for both interstitial and intracavitary source fabrication (figure 1).

We have prototype tested our sources per USASI, 1968, as well as per U. S. Department of Transportation (DOT) "Special Form." While "Special Form" testing was established for transportation needs, it is much more severe than the USASI 1968 tests. The DOT tests are identical to those of the International Atomic Energy Agency (IAEA). Prototype sources were put through these two tests with no failures. (We define failure as increase in removable contamination.) Each prototype source is checked for removable contamination as are production sources, by placing it in water, bringing the water to a boil, removing the source, and taking the water to dryness on a planchet. The planchet is then counted, using normal nuclear measuring equipment.

The sources are measured for output by comparison with a cesium 137 source calibrated by the National Bureau of Standards. We use a Capintec CRC-2 ion chamber radionuclide calibrator for the comparison. The CRC-2 reads out in mCi cesium 137; we use a factor of 1:2.8 to convert this mCi reading to mg Ra. Because of decay, we have established a value of +15 - 0 percent from the ordered value of source strength, to allow for additional source life. The variation between sources in a group shipped at any one time is better than ± 2 percent. Only sources with no removable contamination, using the boil test, are shipped.

A beta scan of unencapsulated canes shows the average deviation along the length is better than ± 3 percent. Beta contribution to the total dose is about 0.2 percent through the Simon Universal Applicator, and 0 through the Simon-Modified Heyman Applicator. The value of 0.2 percent is essentially at the outer surface of the nylon applicator (figure 2).

Both interstitial and the intracavitary sources are color-coded to identify active length, mg Ra equivalent per cm, and year of fabrication. The interstitial sources are coded by three bands near the active end, the intracavitary sources by three dots in the inactive handle. Color coding is done with vitreous porcelain enamel (figure 3).

APPLICATORS

The Simon Universal, Modified Heyman, and Interstitial Afterloading Applicators are all made of nylon. The tubing is specially extruded to a diameter less than 2 mm, and the end pieces are injection-molded nylon. The assembly is done using commercial adhesives as well as ultrasonic welding. The strength of these bonds is equal to the strength of nylon. All three applicators are constructed to prevent contact between the sources and body tissue or fluids. These applicators are supplied prepackaged and sterile, with a relatively stiff stainless steel obturator for insertion.

The Simon-Modified Heyman Afterloading Applicator is about 30 cm long with a 6 mm diameter and a 15 mm long closed bulb at one end. The active length of the installed source starts exactly 2 mm from the bulb end. The other end contains a snap for positive source retention. This locking end is sequentially numbered from 0 to 9 for easy identification during insertion and removal (figure 1).

The Simon Universal Applicator is also 30 cm long, but with only a flat plug to close the end. The active length again starts at 2 mm from the end. The other end has the same snap as the Modified Heyman, and is marked from A through I.

The Simon Interstitial Applicator varies in length according to the length of source to be used. It comes with a conical point and a smaller version of the intracavitary applicator snap. The active length again is 2 mm from the end, and terminates exactly at the shoulder of the applicator. The applicator is grooved for suturing, and the source inactive handle has a hole for suturing or clipping after insertion (figure 3).

CONTAINERS-CARRIERS

The Atomchem Intracavitary Source Container is portable, weighing 75 pounds. It is made of lead-filled stainless steel, and meets all domestic and international regulations as shipping container (figure 4). It can adequately shield 7 sources to a maximum capacity of 120 mg Ra equivalent cesium 137 (figure 5). Radiation level at the surface of the container is less than 2 mr/hr.

The Atomchem Interstitial Source Container is portable, weighs 60 pounds, and is fabricated of lead-filled stainless steel. It meets all domestic and international regulations as shipping container (figure 6). It adequately shields 9 sources to a maximum capacity of 30 mg RA equivalent cesium 137. At this loading, radiation level at the surface of the container is less than 2 mr/hr. Atomchem provides an accessory tungsten shield in the container that reduces the hand exposure rate from 1,000 mr/hr to less than 100 mr/hr.

Each source is placed in a separate tube for ease in identification and replacement after use. The sources may be sterilized by plugging the drain hole in the container side and filling the cavity with appropriate liquid sterilizer, then removing the plug to drain (figure 7).

SUMMARY

Atomchem miniaturized cesium 137 brachytherapy sources are rugged and durable. The single stainless-steel encapsulation, plus entrapment of the cesium 137 in the glass cane, completely protect against radioactive leakage. Only sources that have no removable contamination, as determined by the boiling-water test, are shipped. The 18-gauge size of the source lends itself to the Simon afterloading systems.

Simon disposable afterloaders are small, and can be used alone or in standard applicators which may require minor changes.

REFERENCES

1. SIMON, N., S. M. SILVERSTONE, AND L. C. ROACH: Afterloading Heyman Applicators. Presented at the Meeting of the Groupe Europeen de Curietherapie, Oxford, April 19, 1970.

2. USASI N5.10. Classification of Sealed Radioactive Sources. 1968.

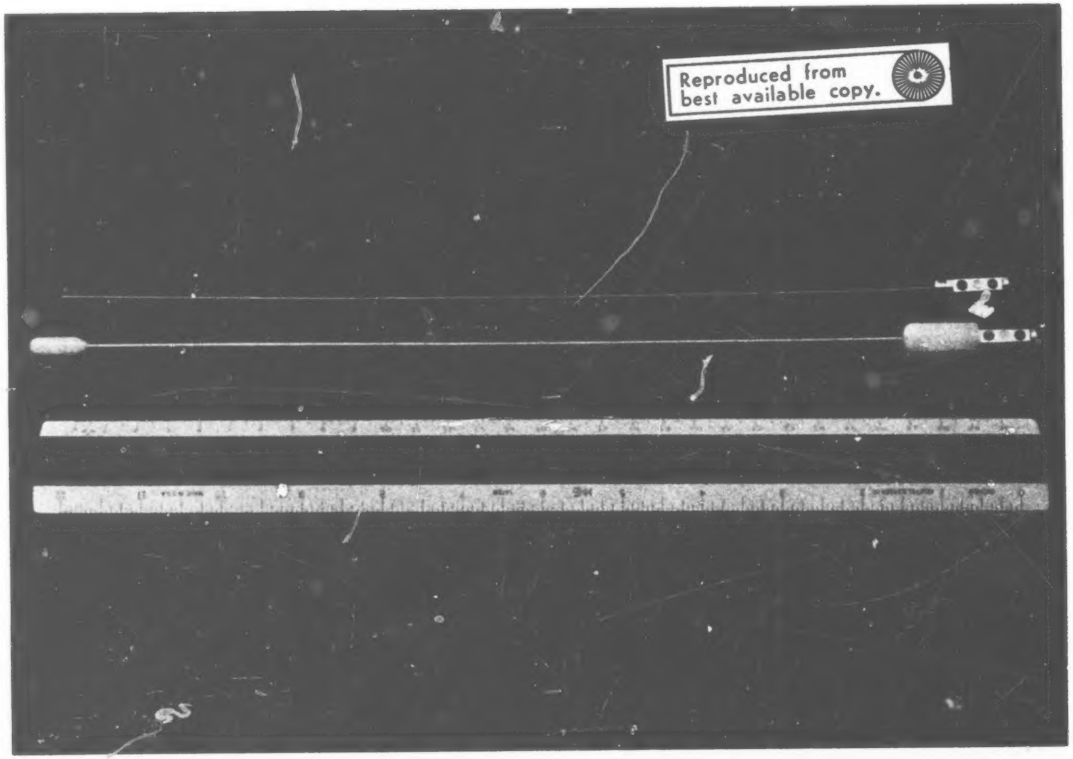

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Figure 1. Simon-Modified Heyman afterloading applicator using Atomchem intracavitary cesium 137 miniaturized source

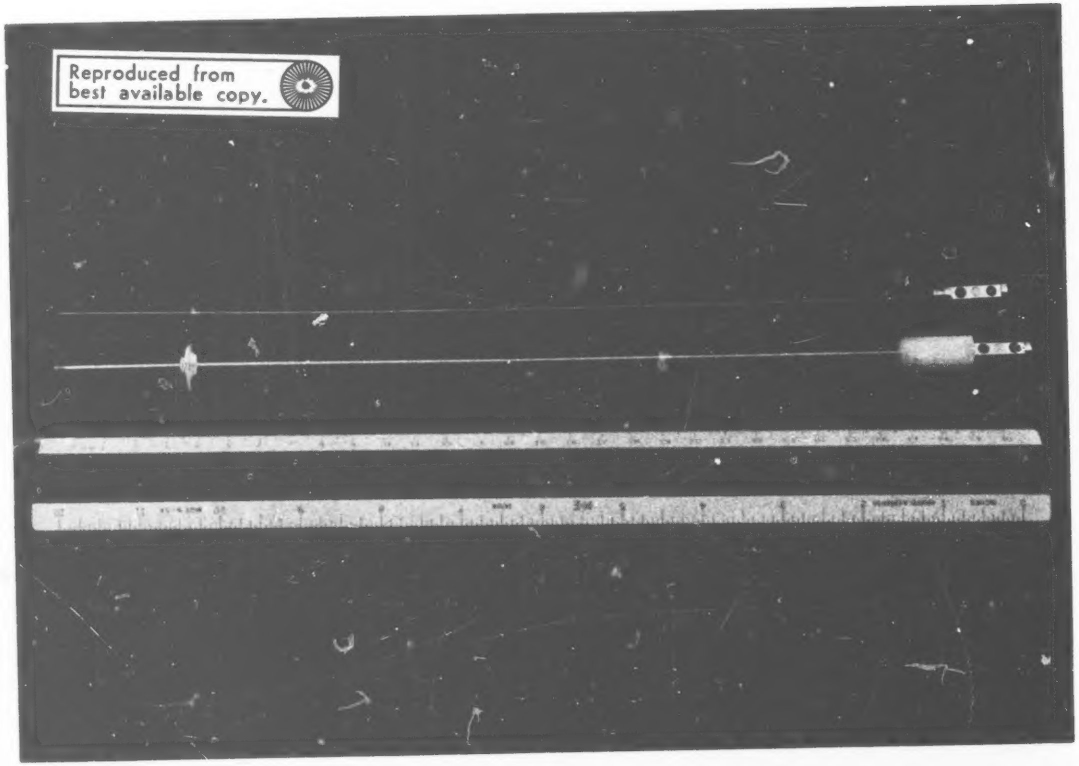

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Figure 2. Simon Universal afterloading applicator using Atomchem intracavitary cesium 137 miniaturized source

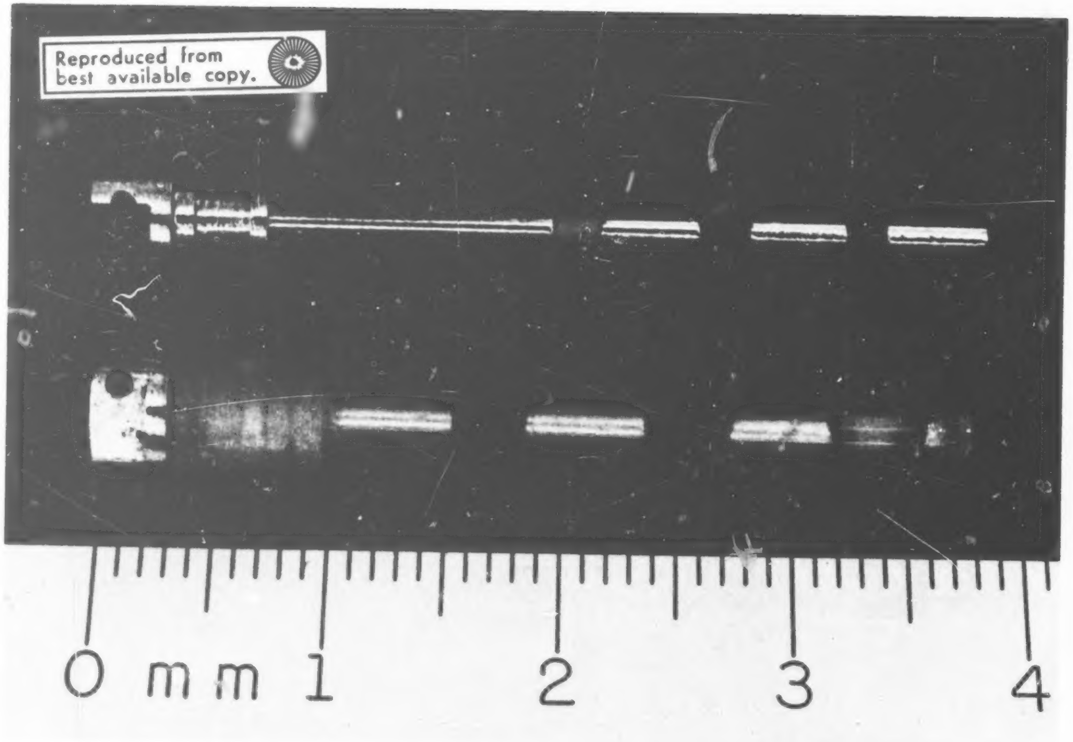

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Figure 3. Simon interstitial afterloading applicator using Atomchem interstitial cesium 137 miniaturized source

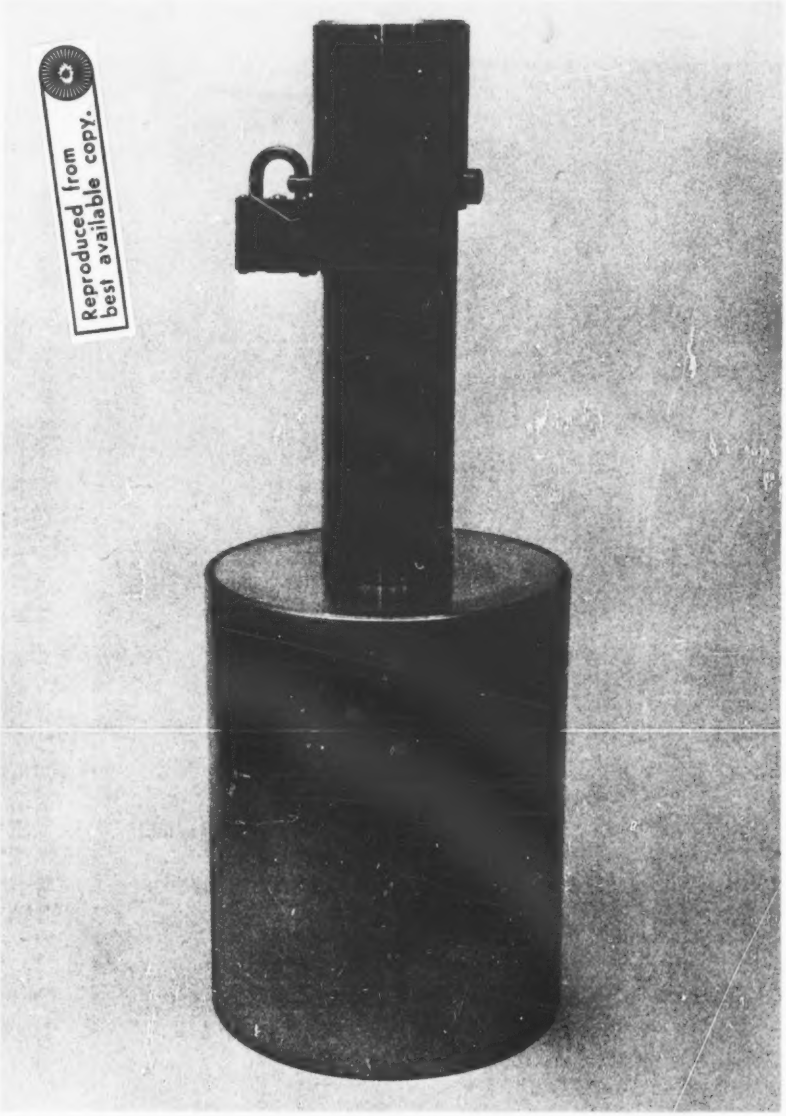

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Figure 4. Atomchem intracavitary source container

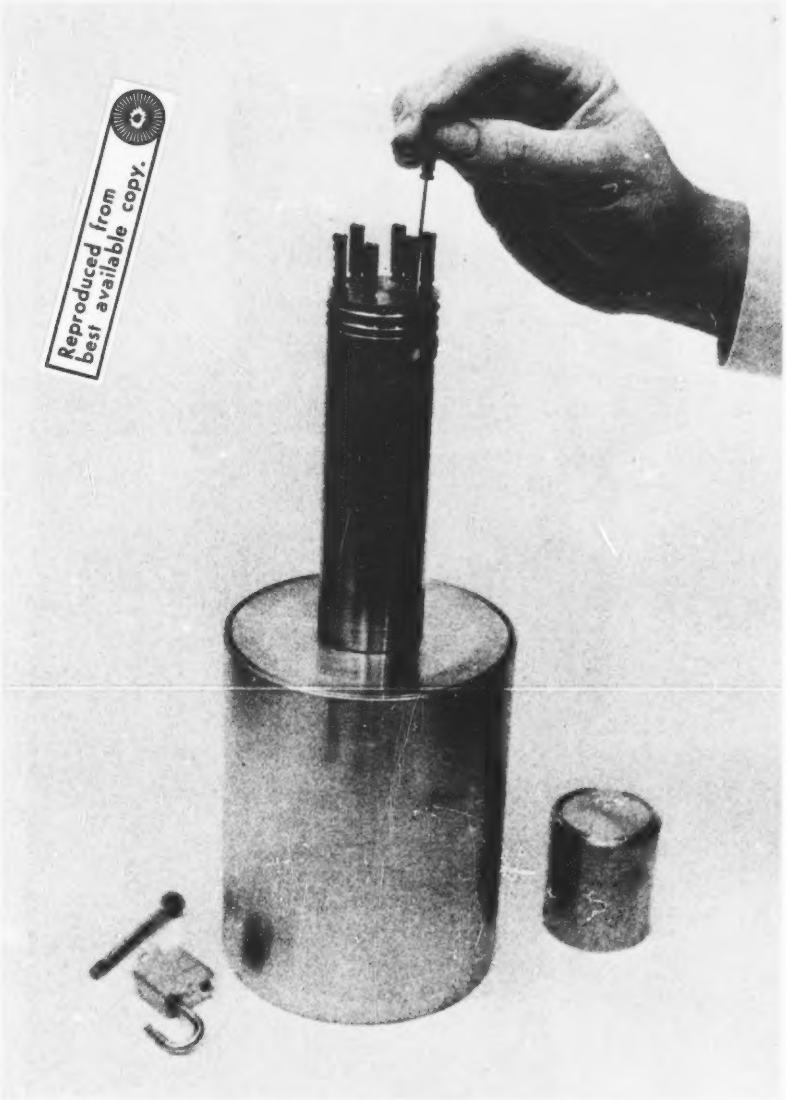

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Figure 5. Atomchem intracavitary source container components

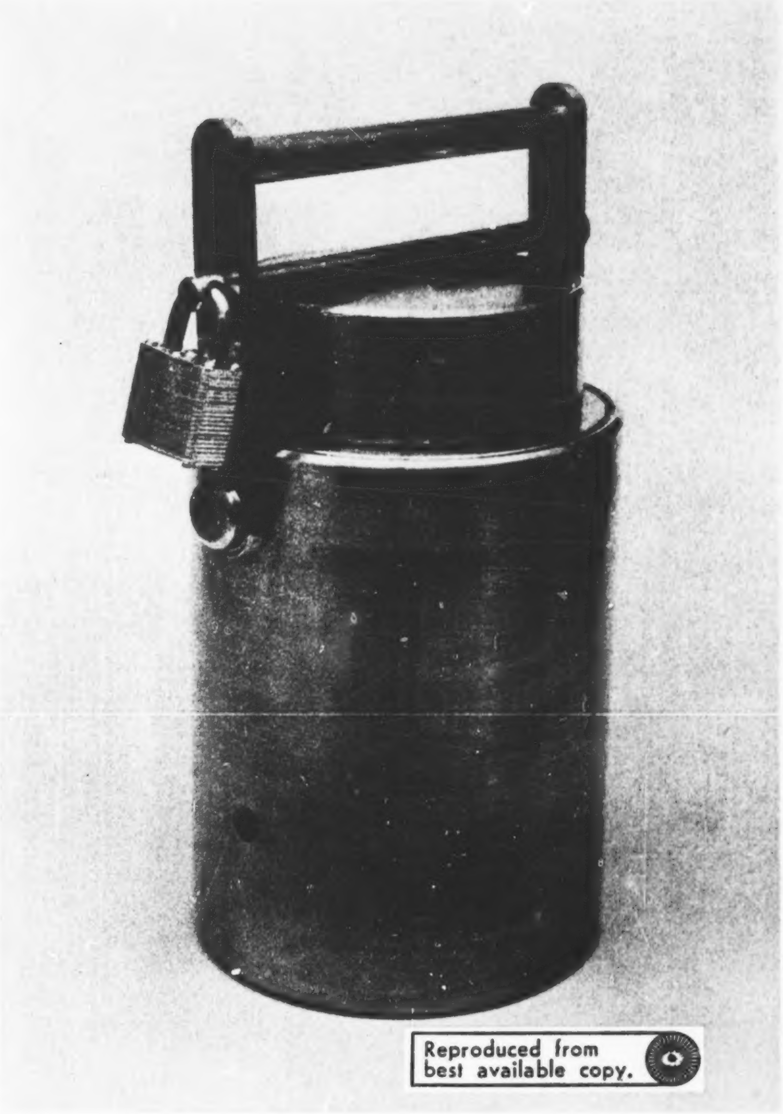

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Figure 6. Atomchem interstitial source container

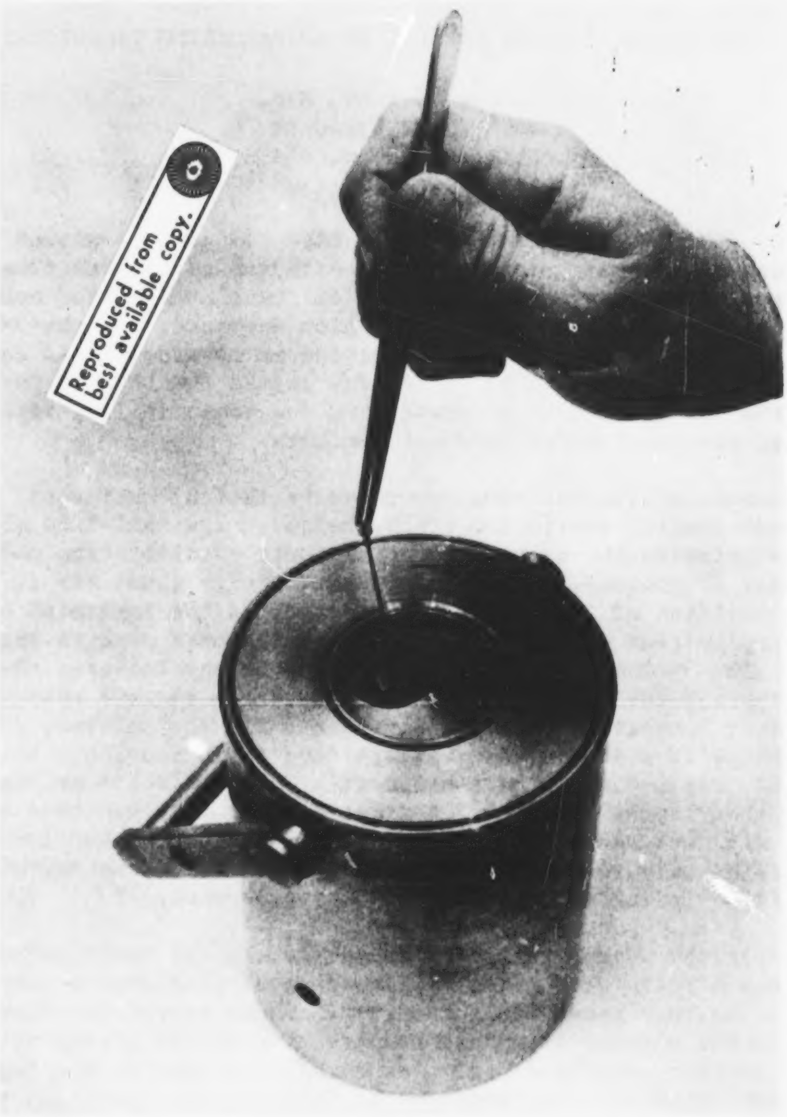

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Figure 7. Atomchem interstitial source container components

CESIUM 137 SOURCES FOR USE IN AFTERLOADING TECHNIQUES

Thomas N. Lahr, M.S.
3M Nuclear Products
St. Paul, Minn. 55101

The two most important goals of afterloading techniques are improvement of treatment by allowing the therapist greater time in placement of sources, and protection of the therapist and other hospital personnel from avoidable radiation exposure. At the 3M Company these are also our goals and to this end we have developed cesium 137 sources which seem to us to be ideally suited for therapy purposes, both from the standpoint of protection and compatibility with existing (and proposed) afterloading techniques.

Because of its radiological characteristics, cesium 137 seems to be almost ideally suited for brachytherapy. Its half-life of 30 years eliminates the necessity for frequent recalibration and replacement of sources, while its moderate energy gamma ray (0.667 MeV) makes shielding of the sources in storage and the implanted patient much simpler than with other isotopes having more penetrating radiations. The 3M Company approach to brachytherapy includes conversion of cesium 137 into 3M brand microspheres, tiny ceramic spheres that are almost completely biologically inert. In the unlikely instance of breakage of a source, the radioisotope is in insoluble form, and is easily cleaned up without probability of inhalation or ingestion by the individuals involved. A great deal of data has been presented on the microspheres in the past, and it is not our intention to cover this again. Figure 1 is a photograph of the microspheres, with a human hair to indicate the size of the tiny particles.

After the development of microspheres as the basic radioisotope form, our efforts were directed toward developing source constructions of maximum integrity and safety. These properties require, we feel, double encapsulation and conservative design throughout, providing sources capable of safe use by all therapists, not just the most sophisticated. Furthermore, we felt it important that the cesium 137 sources be compatible with existing techniques, and the prior experience and education of the therapist. Examples of the types of sources that we provide at the present time will indicate our progress in developing this type of unit.

The first and most common type we provide are the Model 6D6C capsules, sizes CA and CC (figure 2). These are of conventional appearance, similar in size to the radium and cobalt 60 tubes provided prior to their development. They are manufactured of stainless steel with nickel exterior plating, of welded construction, and are calibrated in terms of milligram radium equivalents. This allows the use of conventional radium dosage tables with the cesium 137 sources.

The units are doubly encapsulated (figure 3), the inner capsule sealed by means of silver brazing, the outer welded. Sources of this construction are capable of withstanding and exceeding requirements of the proposed ANSI (American National Standard Institute) standards. They also meet requirements of the AEC and DOT for special form materials.

Since these units are of conventional size, particularly 3.1 mm in diameter, they are compatible with many existing afterloading techniques. For example, they are compatible with the Fletcher-Suit and Henschke afterloading applicators, as well as being the sources used for fabrication of the tandems and vaginal sources for the Horwitz afterloading system. To our way of thinking this latter approach, particularly the use of preloaded tandems, recommends itself to therapists from the standpoint of reducing significantly the amount of handling of radioactive sources, as well as elimination of any isotope handling facilities. As an example, it would seem that preloaded tandems would be suitable for use in the Fletcher-Suit as well as Henschke tandems, as presently designed.

Because of the interest in smaller diameter sources for use in special applications, we have developed Model 6B6G, size LI (figure 4). This unit has the same length and active length as the standard CA tube, but a diameter of only 1.65 mm. In this type of geometry, it would seem to be ideally suited to applicators of smaller bore, particularly those used for irradiation of the cervical area without dilation of the cervix.

Other types of cesium sources are also available, particularly for interstitial use, in both high- and low-intensity standard needles (figure 5). Of particular interest is the high-intensity needle containing 10 mgm radium equivalent, having an overall length of 22 mm and an active length of 10 mm. The low-intensity needles are available in both half- and full-strength loadings, and would be compatible with any interstitial afterloading system allowing the use of sources with a diameter of 1.65 mm or more.

We think that cesium 137 sources recommend themselves for use in afterloading techniques, and that the conventional sources we have available are compatible with most units likely to find widespread acceptance.

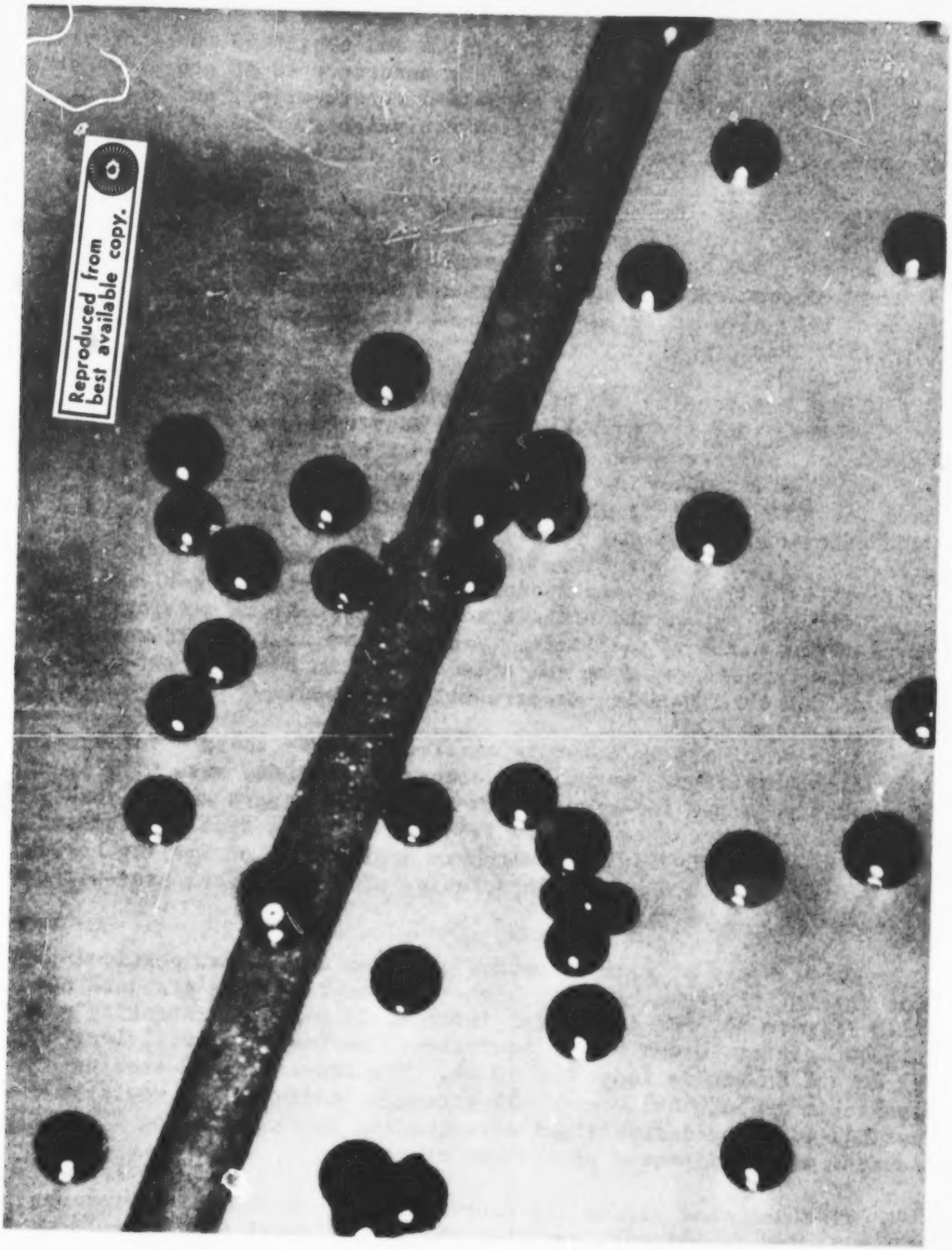

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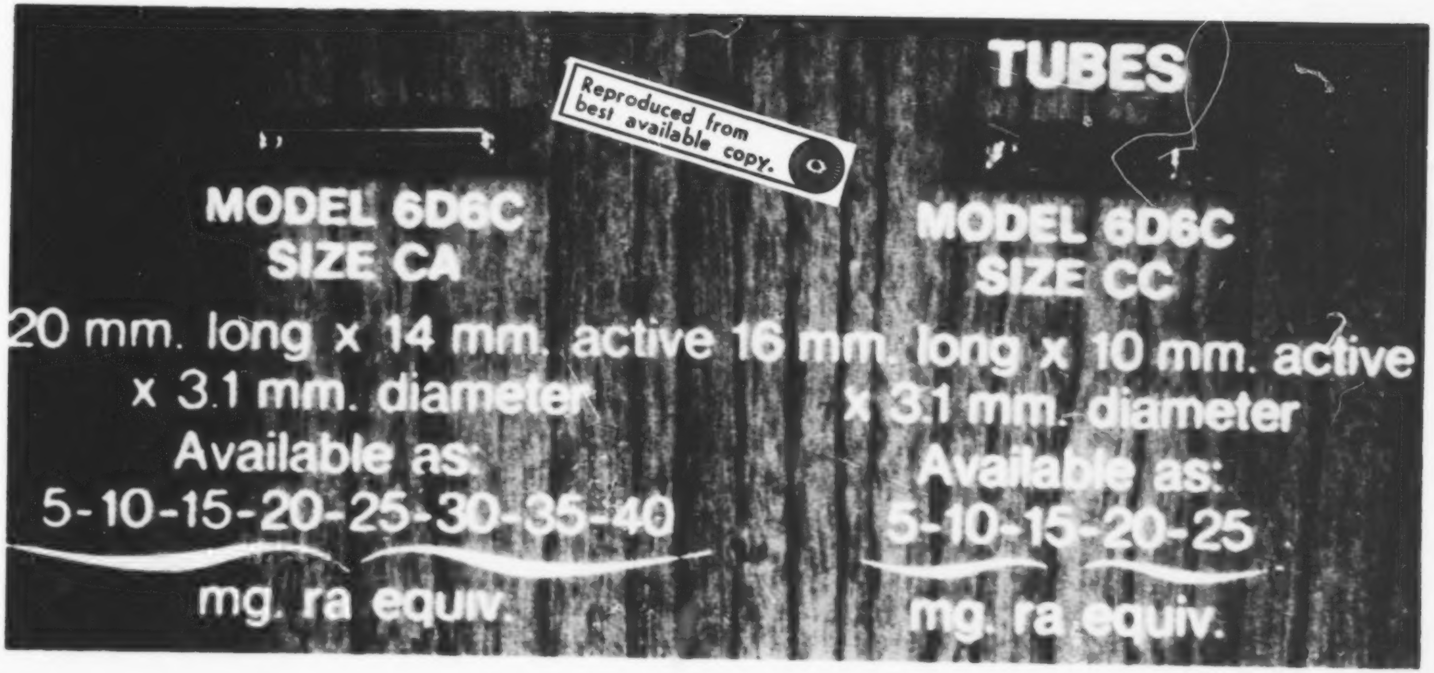
Figure 1. Photograph of microspheres, with human hair for size comparison.



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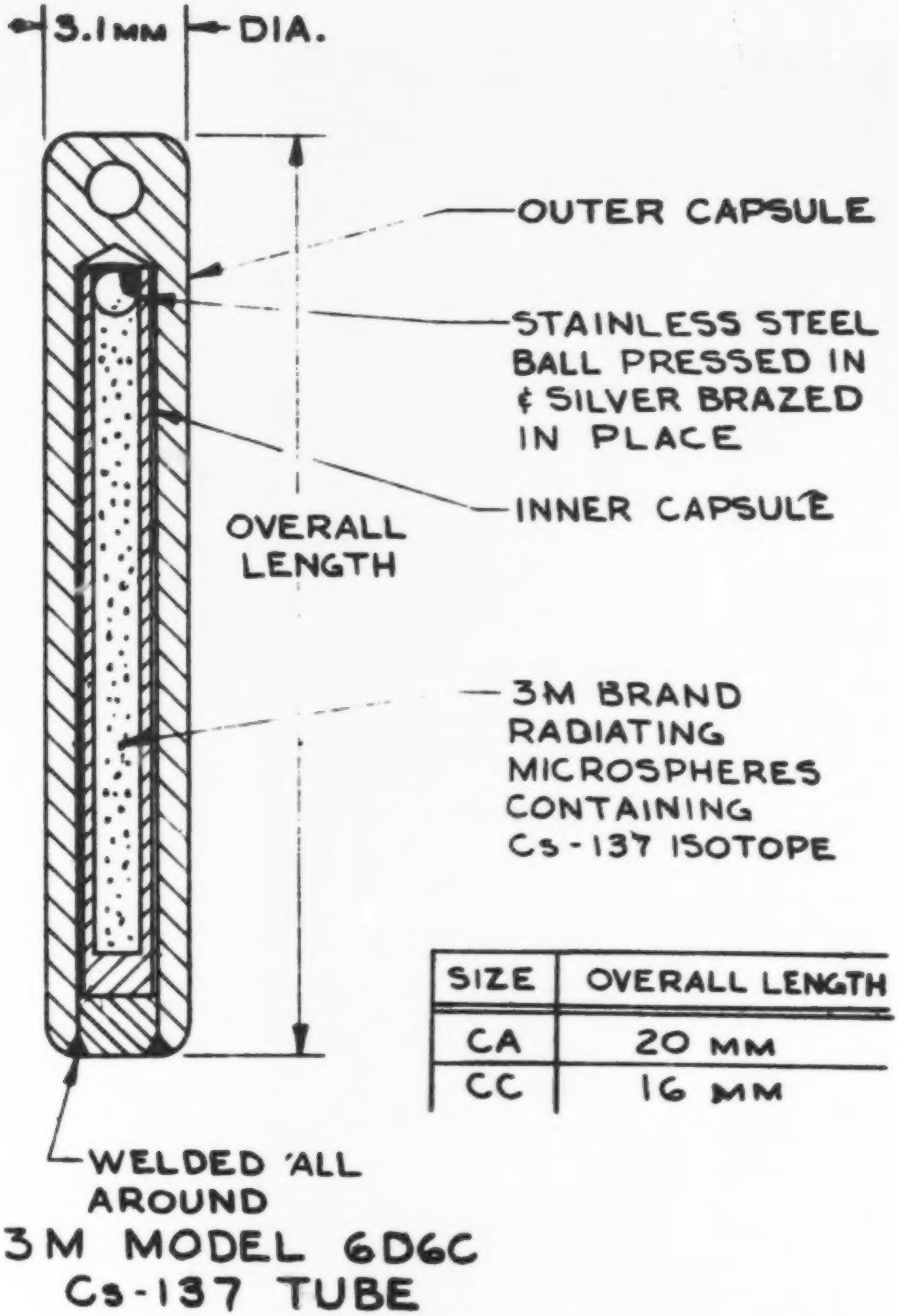
TUBES

MODEL 6D6C
SIZE CA
20 mm. long x 14 mm. active
x 3.1 mm. diameter
Available as:
5-10-15-20-25-30-35-40
mg. ra equiv.

MODEL 6D6C
SIZE CC
16 mm. long x 10 mm. active
x 3.1 mm. diameter
Available as:
5-10-15-20-25
mg. ra equiv.

Figure 2. Comparison of Model 6D6C capsules, sizes CA and CC.


3.1MM DIA.
OUTER CAPSULE
STAINLESS STEEL BALL PRESSED IN & SILVER BRAZED IN PLACE
INNER CAPSULE
OVERALL LENGTH
3M BRAND RADIATING MICROSPHERES CONTAINING Cs-137 ISOTOPE
WELDED ALL AROUND
3M MODEL 6D6C Cs-137 TUBE

SIZE	OVERALL LENGTH
CA	20 MM
CC	16 MM

Figure 3. Internal construction of Model 6D6C capsule.

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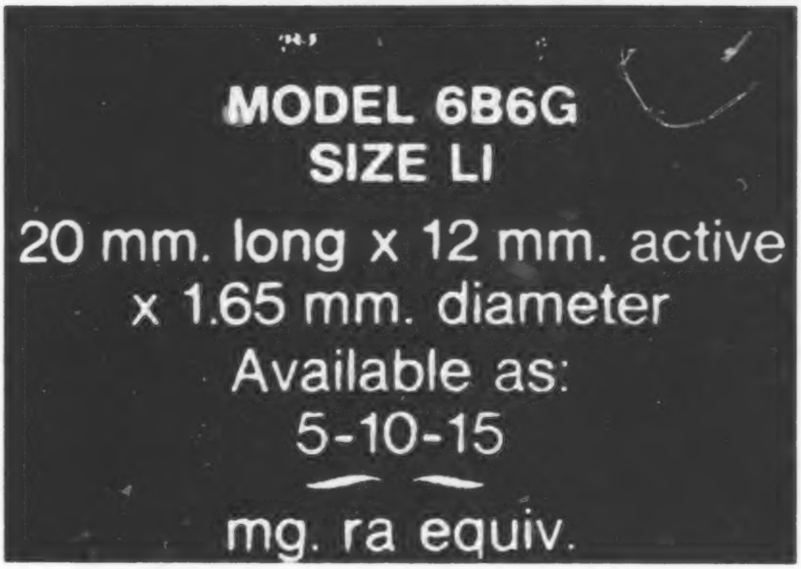
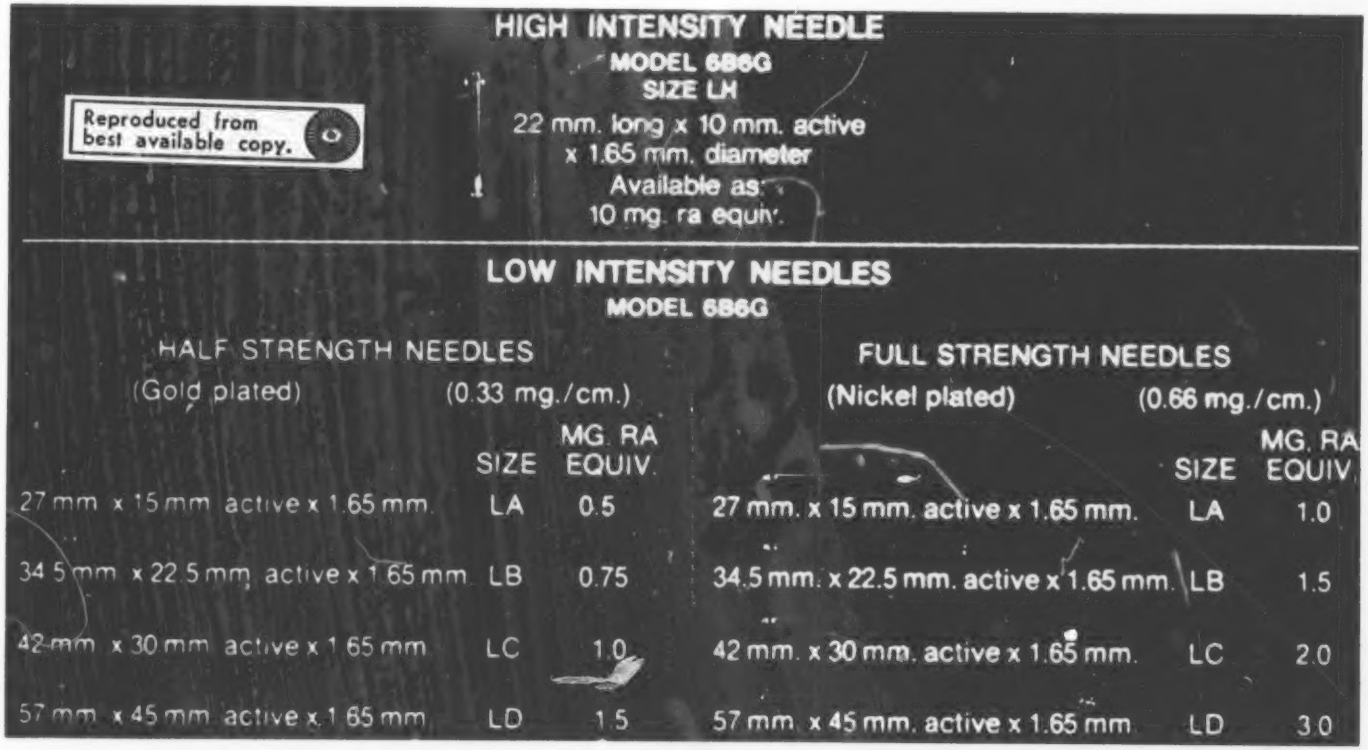


MODEL 6B6G
SIZE LI
20 mm. long x 12 mm. active
x 1.65 mm. diameter
Available as:
5-10-15
mg. ra equiv.

Figure 4. Model 6B6G capsule.



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HIGH INTENSITY NEEDLE
MODEL 6B6G
SIZE LH
22 mm. long x 10 mm. active
x 1.65 mm. diameter
Available as:
10 mg. ra equiv.

LOW INTENSITY NEEDLES
MODEL 6B6G

HALF STRENGTH NEEDLES
(Gold plated) (0.33 mg./cm.)

	SIZE	MG. RA EQUIV.
27 mm x 15 mm active x 1.65 mm	LA	0.5
34.5 mm x 22.5 mm active x 1.65 mm	LB	0.75
42 mm x 30 mm active x 1.65 mm	LC	1.0
57 mm x 45 mm active x 1.65 mm	LD	1.5

FULL STRENGTH NEEDLES
(Nickel plated) (0.66 mg./cm.)

	SIZE	MG. RA EQUIV.
27 mm. x 15 mm. active x 1.65 mm.	LA	1.0
34.5 mm. x 22.5 mm. active x 1.65 mm.	LB	1.5
42 mm. x 30 mm. active x 1.65 mm.	LC	2.0
57 mm. x 45 mm. active x 1.65 mm.	LD	3.0

Figure 5. Cesium source comparison.

CERVITRON-II: AN APPARATUS FOR INTRACAVITARY RADIOTHERAPY

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1212 Geneva, Switzerland

The Gynecological University Clinic of Geneva decided in 1965 to replace the tubular sources of 5, 10, 15 mg of radium by spherical cesium 137 pellets of uniform activity. A varying linear activity is obtained by spacing the active cesium pellets by means of inactive pellets of the same size.

According to the work of Mrs. Dutreix, Physicist to the Institute Gustave-Roussy, the isodose curves at a distance from the central axis equal or greater than 2 cm is the same for a continuous linear source as for a line of point sources spaced not more than 2 cm from each other.

Therefore 6 pellets of 12.5 mCi cesium 137 each give at 2 cm the same isodose as 3 tubes of 10 mg radium. In varying the spacing of these pellets, one therefore obtains the same decreasing linear activity as with an intrauterine tube loaded with 15, 10 or 5 mg radium. By spacing the first pellet at the end of the tube, the treated volume is increased.

This principle of alternating active and inactive pellets as desired has allowed us to construct a new afterloading apparatus, the CERVITRON-II (figure 1), which makes it possible to produce all possible combinations of one type of source, and thus to obtain the isodoses best suited to each individual case. In this way one avoids manipulation of the radioactive substances in the laboratory, and need for a large stock, as would be the case with devices based on prearranged sources.

The radioactive and inactive pellets are stocked in the apparatus behind full lead protection, which contains also the mechanism for composing the lines of sources. The apparatus is connected by cables to applicators previously inserted into the patient. The transfer of the sources into the applicators is done by means of compressed air in less than a half a second; it is controlled by a remote control box outside the ward. At the end of the prescribed treatment time the lines of sources are automatically transferred back into the intermediate safe. From there they are sent into a sorter which separates the active and inactive pellets into their respective safes.

This unit is constructed for 6 applicators. If one wants to use the Manchester technic, i.e. one tandem and 2 ovoids, 2 patients can be treated simultaneously. There are therefore 6 circuits, each with its own time clock. It is possible to use different treatment times for each applicator. If a treatment is carried out by means of several applicators, this allows the operator to adapt the irradiation better than by spatial distribution of the sources only. On the programing panel is a line of 48 holes for each applicator circuit. Each hole corresponds to a pellet: an empty hole to an inactive pellet, a hole with a peg to a radioactive pellet. The apparatus prints a sheet indicating the final composition of each line of sources. The spherical pellets have a diameter of 2.5 mm; the length of each line source is 12 cm.

The usual load of radioactive material in the CERVITRON-II is 36 sources of 30 mCi cesium 137 each, which allows 20-30 hours for each treatment. It is possible, however, to obtain sources with an activity up to 60 mCi.

The active pellets are contained in a completely closed circuit (applicator-transfer cable-safe). Radioactive contamination therefore is impossible.

Colored light signals indicate the position of the sources at any time. The treatment is automatically interrupted and an alarm signal is set off if an unforseen event occurs; for example, power supply failure.

Our aim is to offer a mobile apparatus that permits the radiotherapist (1) to use his own proven method, and (2) to carry out treatment in the ward.

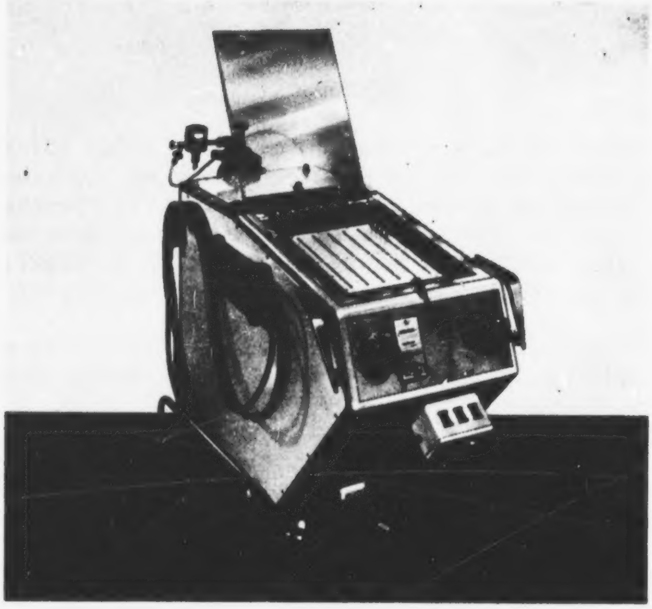

Figure 1. CERVITRON-II: An Apparatus for Intracavitary Radiotherapy

THE CURIETRON: A REMOTE AFTERLOADER FOR GYNECOLOGICAL INTRACAVITARY THERAPY

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AGS
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Levallois, France

INTRODUCTION

The Curietron is a remote-source afterloader for treatment of cervix carcinoma, and can be used with many of the standard applicators with little or no modification (Chassagne, Fletcher, Delouche, Manchester, etc.). The main task set was to produce an apparatus that would give maximum security, ease, and efficiency, yet change as little as possible customary and well-tried medical techniques.

It is the result of 4 years of close collaboration between two teams of curietherapists[1], the French Atomic Energy Commission, and the A. G. S. Company.

For our own part, the A. G. S. Company benefits from 20 years experience in research, development, and marketing of remote controlled isotope projectors, and thus is able to put its accumulated knowledge at the service of the Curietron program.

We are, none the less, happy to acknowledge our indebtedness to pioneers in the field: Messrs. Henschke, Fletcher, Suit, Horwitz, Walstam, Cardis and others without whose work our present achievements would not be possible.

TECHNICAL SUMMARY

Projector

The Curietron system may be broken down into 3 basic elements. The remote controlled Projector, in the form of a four-wheeled trolley contains the electromechanical transfer system, a depleted uranium storage safe, and the control panel.

The Curietron weighs around 100 kilograms and is easily moved. Handrails and shock absorbers protect it from bumps and jolts.

---

[1] B. Pierquin and D. Chassagne, Institut Gustav-Roussy, Villejuif; and J. Gest and G. Delouche, Centre Rene Huguenin, Saint-Cloud.

Figure 1 shows the remote control unit (1) being operated. Commands are transmitted to the cable motor-drive (6). This drives the source holders in and out of the depleted uranium storage chamber (3), along the four ejection sleeves (4) and into the applicator(5). The projector control panel is shown at (2).

The remote control unit will normally be placed at the entrance to the treatment area and comprises operational push buttons and positional indicators: red for source holders in the treatment position, green for source holders in the storage position. A yellow indicator operates when the source holder is in the course of transfer from one position to the other. In fact, as an essential guarantee that irradiation is taking place in the correct predetermined treatment position, a switching device insures that the red indicator will only light up when the source holder has reached the very end of the ejection sleeve corresponding to its proper location in the applicator.

The projector control panel duplicates the source position indicators (red, yellow, and green) already found on the remote control unit and also features the 4 independent treatment timers, one associated to each ejection sleeve channel. Counting starts when the red indicator lights up, and stops when it extinguishes. Therefore only actual treatment time is totalized.

Source and source holder

The next essential element in Curietron design philosophy is the source and associated source holder (figure 2).

The source consists of a grain of cesium 137 in the form of a high melting-point ceramic hermetically sealed in a stainless steel capsule. It conforms to recommendations of the International Atomic Energy Agency regarding special sources, and is supplied by the French Atomic Energy Commission.

The capsule measures 3.5 by 1.5 mm diameter. The cesium grain itself measures only 1.6 by 0.8 mm diameter.

Source holders are preassembled with a sequence of source capsules and inactive spacer bearings to give a range of differing active lengths. Each grain has an activity of 12.5 mCi, and total source holder activity can vary between 12.5 and 150 mCi over active lengths from 8 to 96 mm. More concentrated activities are possible by reducing the number of spacer bearings and by using grains of higher specific activity.

Overall source holder length is 35 cm with a diameter of 3.2 mm.

Containers

Though the Curietron Projector is a storage container in its own right with a surface dose of only 2.5 mR h when charged to capacity, for utmost flexibility it is best used in conjunction with a separate storage and transfer container. This comes in two versions: the 4L container with 4 storage channels (figure 4), and the 20L container with 20 storage channels.

These make it possible for the user to choose the most suitable set of source holders for a particular treatment from a large stock selection. Transfer from container to projector is effected by means of a special transfer sleeve.

The 4L container may be dismounted from its trolley and used for source transit purposes. It conforms strictly to type B international transport regulations.

MANUAL AFTERLOADING

In the initial stages of equipping a center, and to allow users to become fully conversant with the afterloading principles before adopting the remote loading procedure, the 4L and 20L containers may be used as treatment aids in their own right; that is, for the purposes of manual afterloading.

Whereas security is considerably increased in being able to wheel the storage safe right up to the bedside, advantage can also obviously be taken in preparing the patient in the "nonradioactive stage" which is, after all, the basic afterloading principle. Once the applicator has been inserted in the patient and the situation checked through the use of dummy source holder and radiograph, the active source holders are extracted from the mobile storage container at the last moment and placed smoothly and rapidly in the applicator.

The Delouche plastic applicator, ingeniously simple in design with only 6 different geometric configurations, if used in conjunction with the source holders already described, makes possible the use of precalculated isodose curves. This considerably facilitates dosimetry. Coupled to manual afterloading, it enables users who so desire to start in a modest way. As all the equipment is fully compatible, the full benefit of the remote facility can be added at a later date.[2]

---

[2] The Delouche applicator is primarily designed for use in remote afterloading. In this context, it may still be used to advantage in conjunction with precalculated isodose curves. The occasion may also arise to use the containers with other applicators for the purposes of manual afterloading.

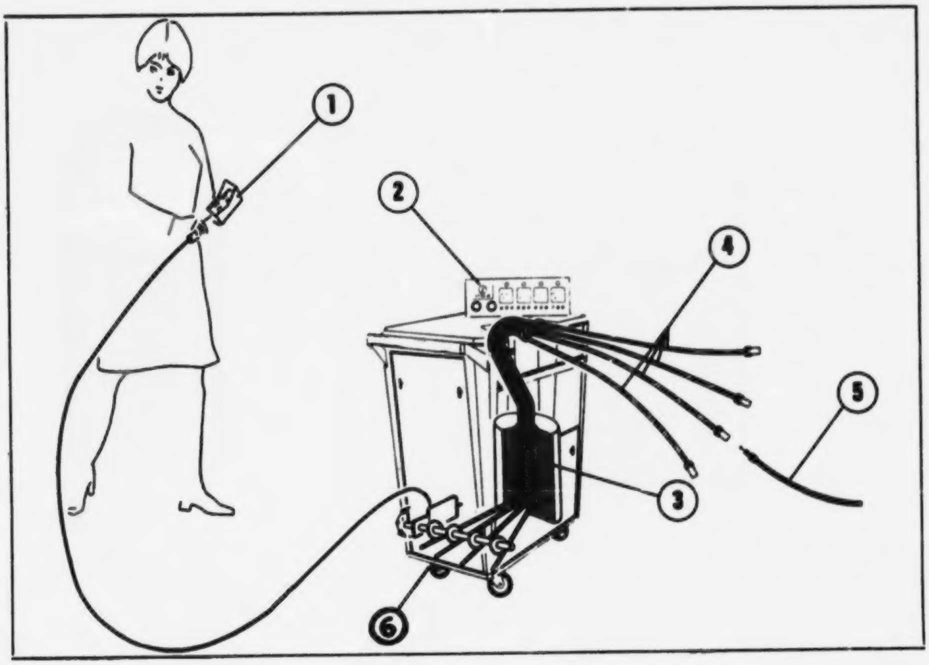

Figure 1. The remote control Curietron projector

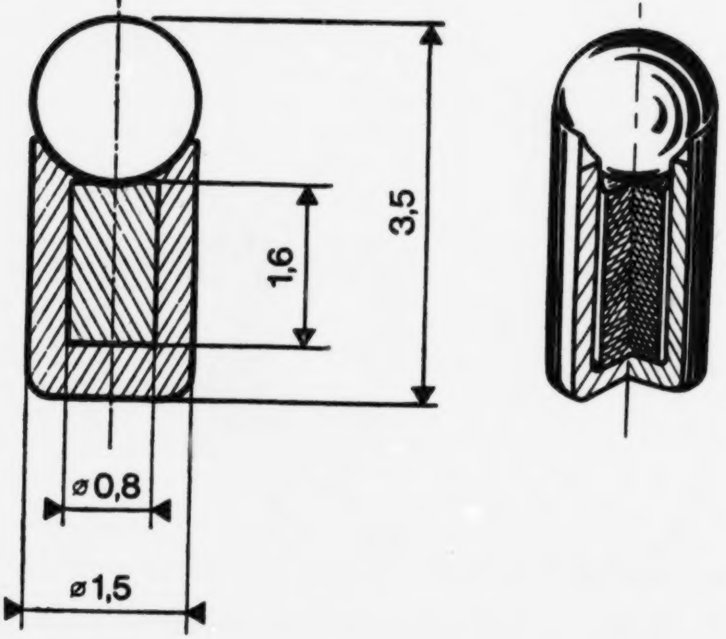
3,5
1,6
ø0,8
ø1,5

Figure 2. The source and source holder

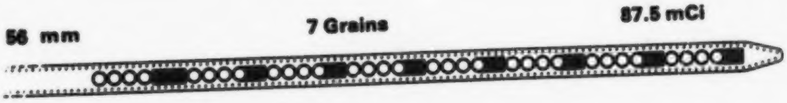
56 mm
7 Grains
87.5 mCi

Figure 3. Example of active end of source-holder

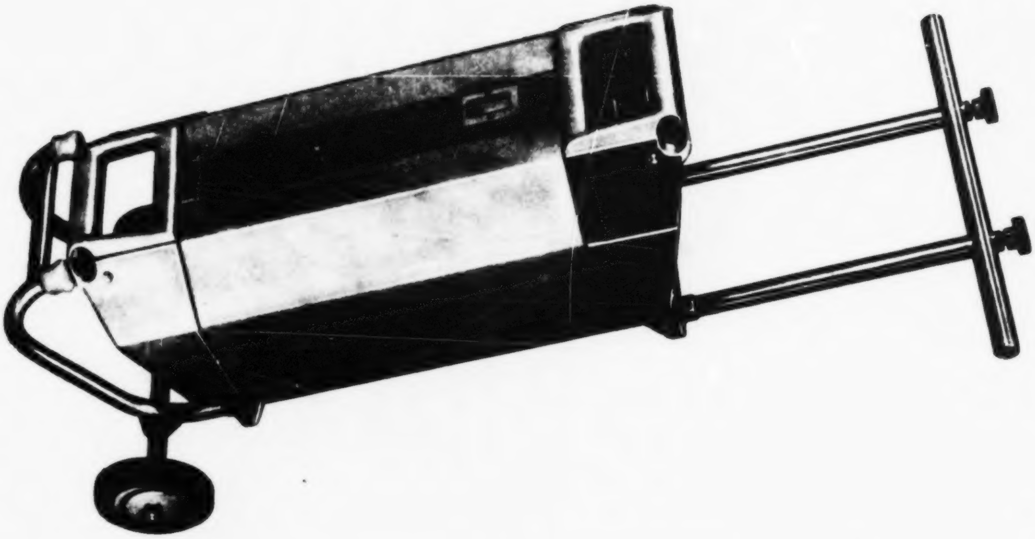

Figure 4. The 4L container with 4 storage channels

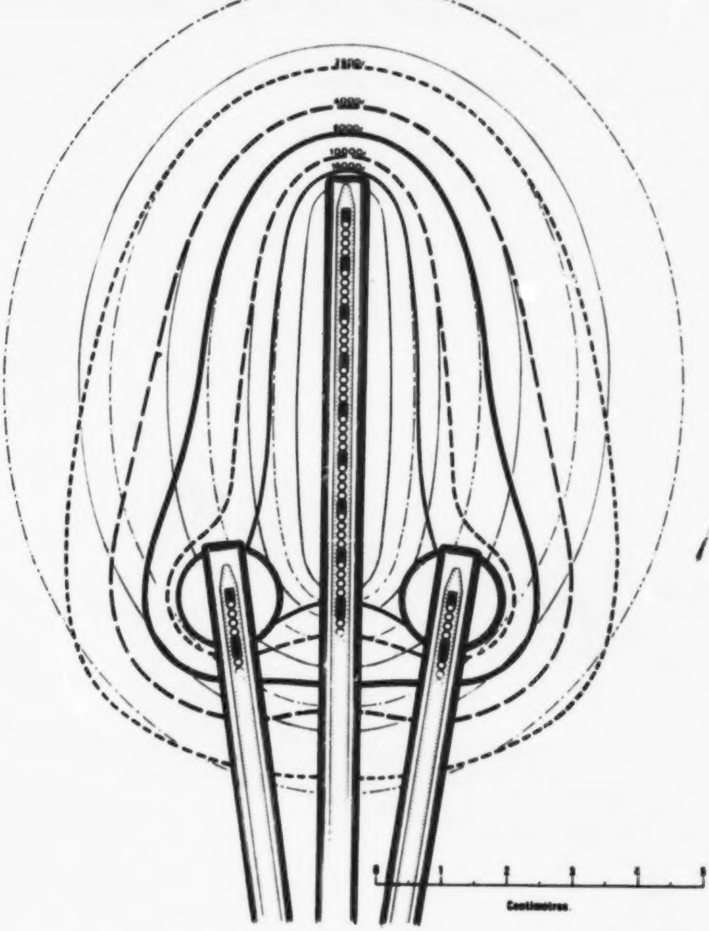

Figure 5. Example of precalculated isodose curves for use with Delouche applicators in conjunction with A.G.S. source holders

(courtesy of the Radio-Physics Department, Institut Gustav-Roussy, Villejuif)

AFTERLOADING EQUIPMENT

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This conference has covered the development of afterloading techniques from the radiation dosimetry and the clinical aspects and by outstanding authorities, in perhaps the most comprehensive program on these subjects ever held. I will attempt to show some of the major afterloading applicators that are presently available, particularly those produced by our company, and to present some mechanical details and problems that may be of interest or concern to the users of these devices. I will also discuss a few practical considerations taught us by experience.

The earliest development of afterloading applicators probably was sytems that enabled radon implants (seeds) to be introduced without the need for individual implantation of single seeds with inserting needles. These early techniques have culminated in presently available preloaded ribbons or carriers for several isotopes, notably iridium, and notable developments in afterloading techniques with radon by Dr. Oscar Morphis.

Intracavitary applicators developed by Drs. Fletcher and Suit at the M. D. Anderson Hospital, Houston, Texas, have had wide acceptance and have notably advanced the state of afterloading. Figure 1 shows the overall appearance of the applicator -- the ovoids and the source carriers, the available tandems, and the plastic tubes and rods used as source carriers in the tandems.

Figure 2 is a cutaway depicting the interior construction and mechanical principles by which the source fits into the vertical plane of the ovoids. The lead shielding segments prevents excess radiation in various directions.

Figure 3 is the Henschke applicator, in which the ovoids are in a horizontal plane. This configuration results in a simpler design of source carrier and positioning, as the same plastic tube and rod used in the tandems can be used in the ovoids. One other design feature is the locking clamp that holds the two ovoids and tandems in a fixed position.

Figure 4 is a modification of the Henschke applicator using the thin tandems developed by Dr. Gordon Ridings. The smallest ovoids (2.0 cm diameter) of the Henschke applicator are used in conjunction with tandems of the smallest possible dimensions, resulting in an applicator of minimum dimensions amenable to afterloading.

Dr. K. Charyulu has demonstrated models of a low-cost afterloading cervical applicator in which most of the parts can be made disposable.

Perhaps the most comprehensive afterloading device available is the Delclos uterine vaginal applicator. The variety of segments and system of assembly of these segments allows for great variation in dimension to suit the anatomy (figure 5).

The Burnett afterload vaginal applicator is another system in which great variation in applicator dimension can readily be accomplished. The length of the afterload holding device and ease of insertion of radioactive sources reduces radiation exposure to a minimum.

One practical consideration that should not be overlooked is the matching of radioactive source sizes with the available applicators. For the Fletcher-Suit applicator, the largest source dimension is 20 mm external length by 4.05 mm external diameter (the British "G" type radium tube). These tubes require a special thin-walled plastic source carrier, whereas the standard radium tube sizes are more readily loaded in the standard source carriers. Tubes of larger dimensions cannot be used because of the clearance necessary to change the angulation of the tube and source carrier as it is moved into the ovoid.

The 4.05 mm diameter also is the maximum that can be used for the standard Henschke applicator. The Ridings applicator can be used only with radium needles, or sources smaller than 1.75 mm diameter.

Two other very practical considerations are the sterilization systems and the control of the radioactive materials, especially during removal of sources at the end of the treatment. Steam or other high-temperature sterilization methods should not be attempted on the plastic parts of the various applicators. In some cases loaded tandems have been sterilized by mistake, yielding a melted plastic mass inside the tandem. A difficult and hazardous task to recover the radioactive source is the result.

Adequate procedures for radiation safety and control of the sources should be provided, for the sources often are scheduled for removal at late night hours and in areas away from normal radiation supervision. Proper carriers and transport carts are a great aid.

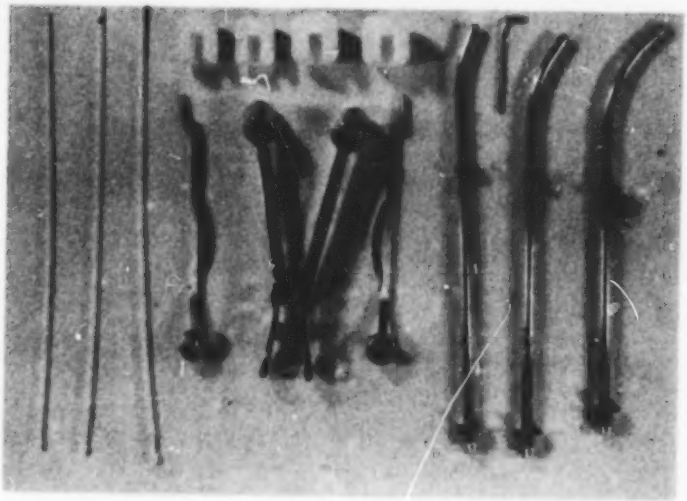

Figure 1. Overall appearance of the applicator (Fletcher-Suit).

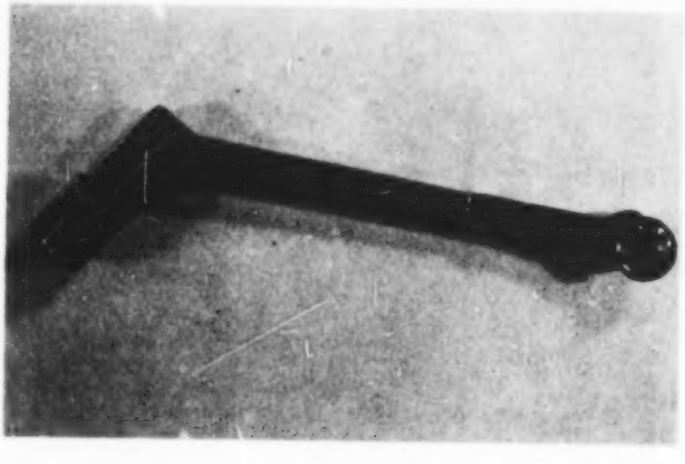

Figure 2. The interior construction and mechanical principles by which the source fits into the vertical plane of the ovoids (Fletcher-Suit).

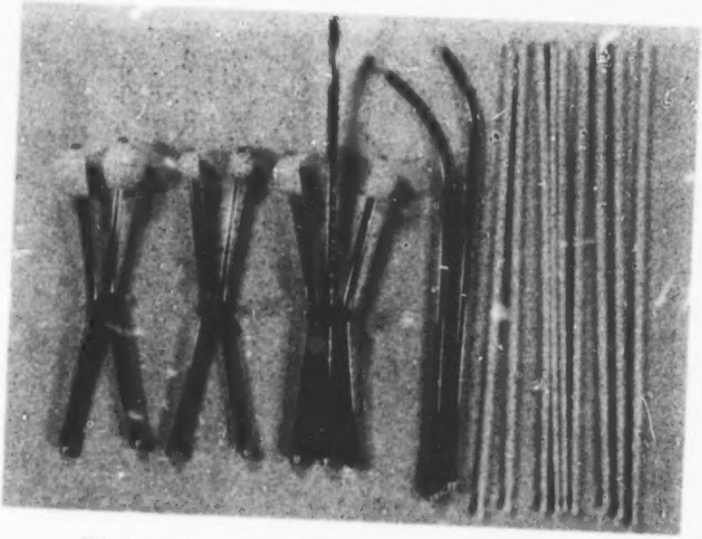

Figure 3. The Henschke applicator.

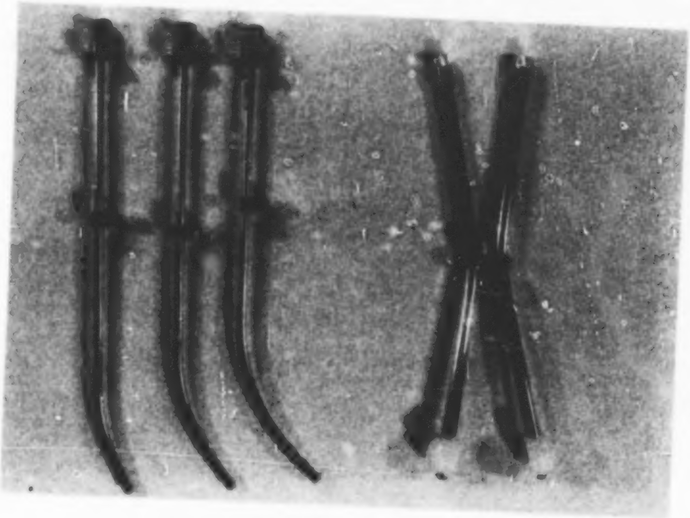

Figure 4. A modification of the Henschke applicator using thin tandems.

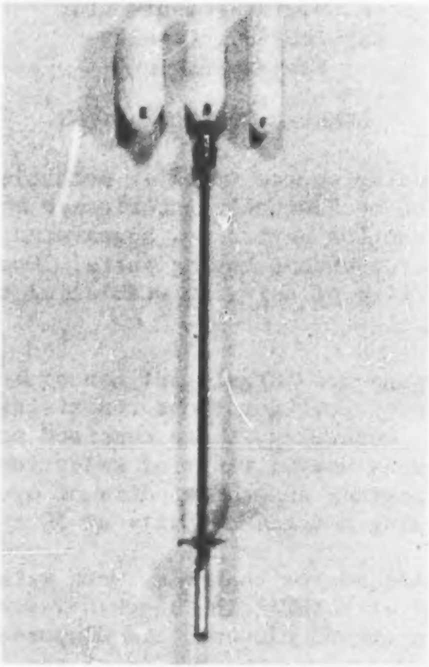

Figure 5. The Delclos uterine vaginal applicator.

THE CATHETRON

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Sussex, England

GENERAL CONSIDERATIONS

A study of existing source transfer mechanisms showed that a complicated system of mechanically interlocked shutters was generally used, and that malfunction hazard was aggravated by a relatively large number of interdependent moving parts. Consideration then was given to the possibility of using an undulating channel to accomplish radiation shielding.

The initial design was largely influenced by the desire to follow existing Manchester configurations comprising a uterine applicator and two ovoids. Generally, three combined source distributions are used. To provide a useful range of selection, it was decided that three uterine sources and three pairs of ovoid sources should be incorporated, giving a total activity of 50 curies of cobalt 60.

Thus we have nine source channels, each with a double curve leading into and out of a shielding block. These nine channels are arranged so that the curved elements are disposed radially about the central line and bend towards the middle of the block. With 50 curies cobalt 60 concentrated at the center, the shielding required took the form of two hemispherical castings bolted together and filled with lead. Measurements have shown that the maximum surface dose rate at this loading is 2 mR hr.

DRIVE MEANS

A commercially available drive system, marketed under the name TELEFLEX, was chosen and adapted to our requirement. This consists of a double layer of high tensile steel wire on which is wound a helix of spring steel wire under tension. Gear boxes, available from the TELEFLEX Company, are designed to mesh with the outer helix of the cable to provide a positive nonslipping drive. In the finalized design, double gear boxes are used: one acting on the drive cable, the other on the indicator cable at half the drive cable's gear ratio. The source position thus is indicated at the control console in half scale, and is solidly connected to the drive cable via the double gear box.

THE SOURCE PENCIL

Because of the requirement for extreme mechanical flexibility, a spiral spring envelope was developed to house the source capsules. In cooperation with the Radiochemical Centre at Amersham, suitable sources were developed. These were based on a 1.5 mm diameter cobalt wire 5 mm long, in an inner stainless steel welded capsule. Subsequent to irradiation, the inner capsule was welded into an outer stainless steel capsule whose overall dimensions were 3 mm diameter and 8 mm length, with domed ends.

The spiral spring envelope will accept up to 12 capsules, either active or dummy brass blanks. A wide range of isodose distributions can be achieved, depending on the number and activity of the sources, and the number and distribution of blanks. The purpose of the millicurie sources is to use them as measuring monitors to check dose rate distributions, particularly in gynecological applications where the rectal dose is monitored by means of a rectal probe.

The shaft end of the source holder is manufactured from a length of TELEFLEX drive cable, and the total assembly is some 18 inches in length. The drive type cable extends through the end of the source container when the sources are loaded in the safe position. Suitable means are provided to couple any of the source assemblies to any of three drive cables extending to a remote console in a shielded area.

INTERLOCKS

Mechanical interlocks, at the input end of the source container, consist of two hardened steel forks that engage in the helix of the source pencil shaft. These locks are spring loaded and operate in slideway. They can be raised free of the drive cable by means of push rods which operate from each end of the source safe when the input and output connections are screwed into position.

Electrical interlock switches operate in conjunction with the mechanical interlocks to provide remote indication of interlock integrity, and to control electrical relays interconnected in the source drive system.

With the electrical power supply connected, any interlock failure insures that the sources are driven to the safe position. In the absence of the power supply — whether due to mains failure or operation of the source drive supply switches -- the sources are driven to the safe position by gravity, with mechanical indication of the position of the source drive cable at the control console.

In overall configuration, there are 9 source pencils in the safe. Each source loading and disposition is identified by channel numbers. Three drive means are provided in the control console and are designated Red, Yellow, and Blue, respectively. Three drive extend from the control console to the safe, are capable of being connected to any of the source channels by means of a special input connector bearing a similar color coding. Three color-coded flexible output tubes can be connected to the output end of the safe. Each of these tubes is fitted with color-coded quick release connection, fitted with an electrical interlock, and designed to accept any of the applicators available.

At the control console are nine jack sockets numbered 1 to 9, and three jack plugs color coded Red, Yellow, and Blue.

The source configuration for treatment is selected, and the channel numbers identified. Each channel number is allocated a color-coded drive. The appropriate colored jack plugs are inserted into the selected channel jack sockets, and the colored input connectors and drive cable connections to the source pencils are connected at the input end of the safe. Correspondingly colored output connectors are connected at the output end of the safe. Finally, these output tubes are connected to the applicators -- providing that color-coding is consistent with the jack plug selections at the console, and that throughout the system a white signal lamp is illuminated above each associated color channel at the control console, indicating that the interlock sequence is correct.

The source drive supply is controlled by a Yale-type key, kept in the possession of a qualified person responsible for operation of the machine. With the key in the nonoperational position, the system is gravity controlled, with mechanical indication of the source pencil position displayed at the control console. In the operated condition, remote electrical indication is displayed showing safe (green), transit (amber), and exposed (red), together with white indication of interlock integrity.

Violation of the interlock in any condition other than safe causes the source to be driven to the safe position by electrical means.

TREATMENT TIMING

Color-coded preset timers are provided. They commence to run down to zero when the sources reach the treatment position. At the same time, countup type timers are energized whose indication is maintained until mains shut down or the start of a new treatment, thus providing positive information of expired and unexpired treatment times for all channels. When the preset timers reach zero the sources are electrically driven back to the safe position.

GENERAL OPERATION DESCRIPTION

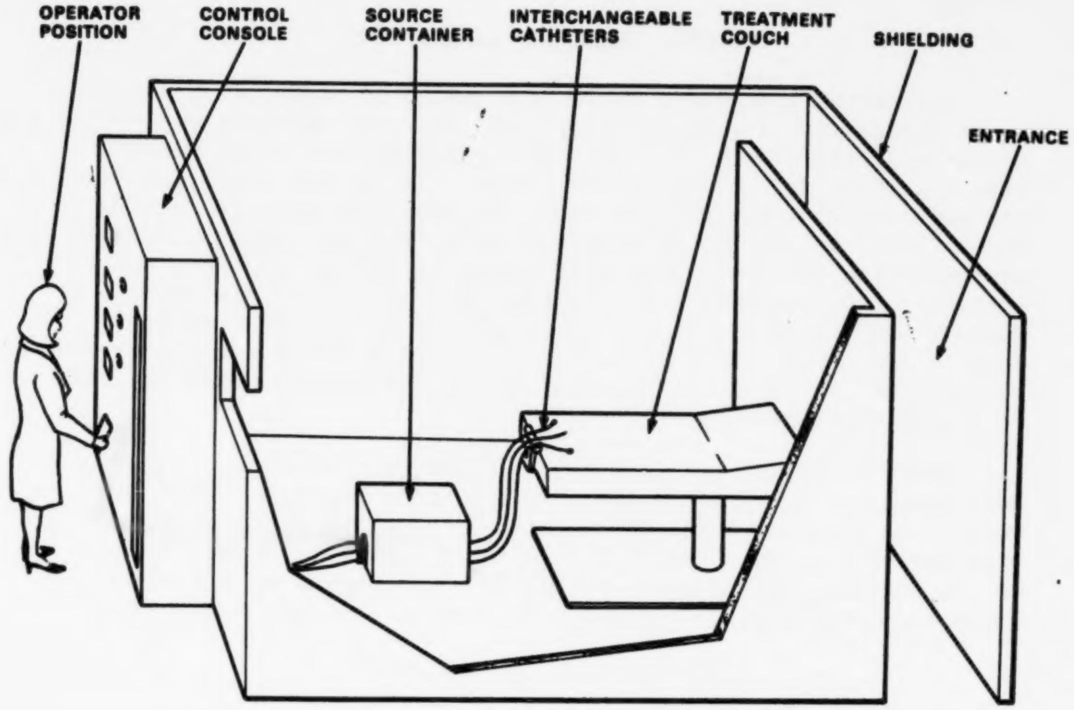
A TELEFLEX type drive cable is actuated by means of an electric motor fitted with a worm and wheel gear box. It operates via an electromagnetic clutch into the cable drive system, which incorporates a gravity controlled return device. In the energized condition, the magnetic clutch transmits the drive when the motor is running and at rest; and transmits torque derived from the gravity control system to the nonreturn worm gear fitted to the motor. When not energized, the magnetic clutch allows the cable drive system to operate under gravity control independently of the drive motor. Thus if any source drive supply is interrupted for any reason -- including failure of the main supply -- the system is gravity operated to a safe condition.

Manual override adjustment in each drive channel is provided over the final 20 cm of travel at the exposed position. This is controlled by a handwheel fitted with an integral manual clutch, together with a push button to reduce the electromagnetic clutch torque during manipulation. If the 20 cm is exceeded, the motor drive is energized, returning the sources to the safe position.

ARRANGEMENT OF THE EQUIPMENT

The disposition of the equipment is illustrated in the diagram on the following page, where it is seen that the patient is located on a treatment table in a suitably shielded room. (Possible configurations for the room are also shown in the diagram.) A number of interchangeable catheters are available and are connected to the source storage container, which is also situated in the treatment room.

The operator controls the treatment from a console outside the treatment room and it is desirable that means of communication are provided between the operator and the patient. It is also desirable that visual monitoring is possible either by closed circuit television or by a radiation proof window.



OPERATOR POSITION
CONTROL CONSOLE
SOURCE CONTAINER
INTERCHANGEABLE CATHETERS
TREATMENT COUCH
SHIELDING
ENTRANCE

ARRANGEMENT OF THE EQUIPMENT

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KEYWORDS: Afterloading; Brachytherapy; Radium; Substitutes; Equipment; Medical Aspects; Dosimetry; Cancer.

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